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1459

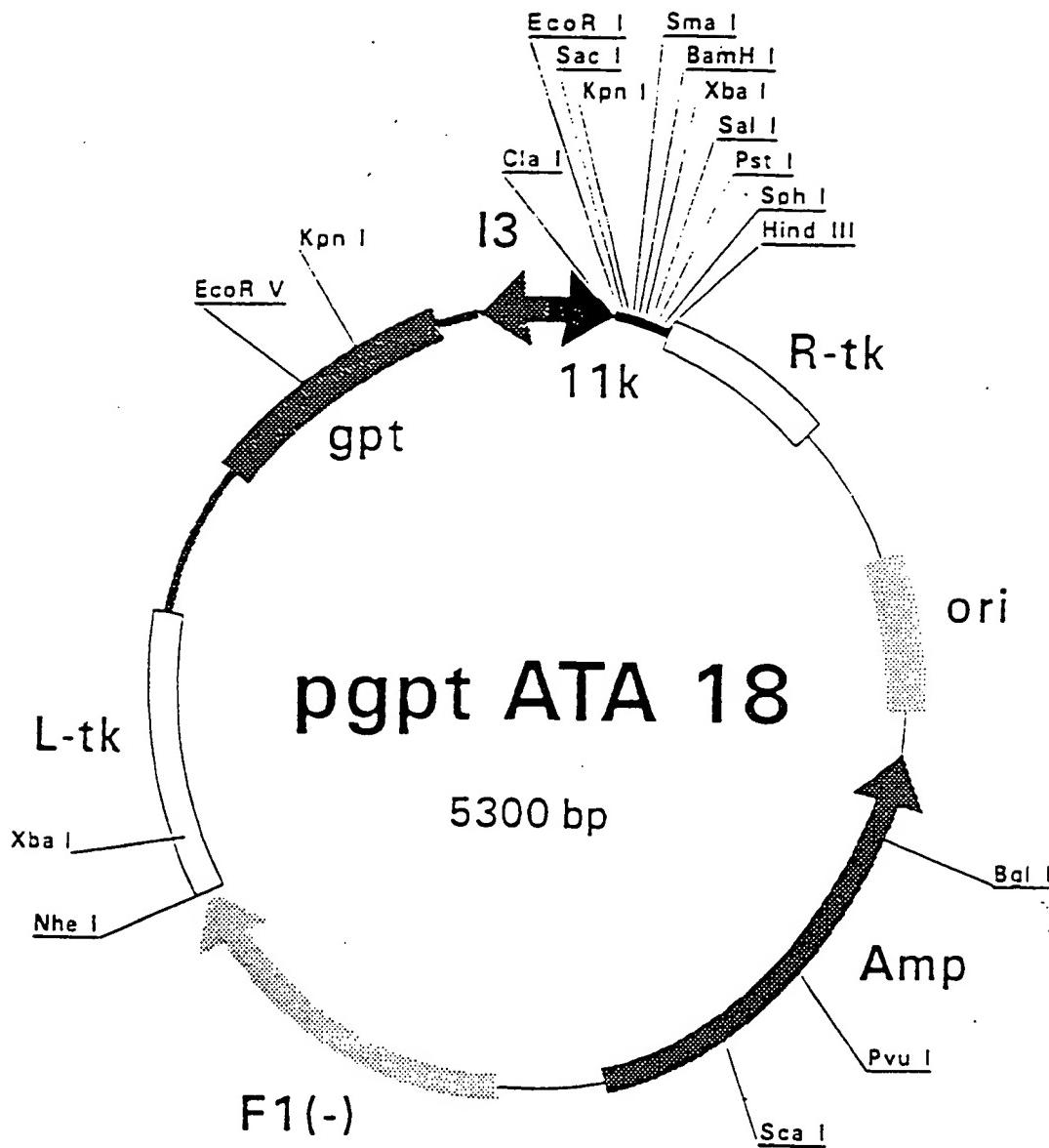


FIGURE 1

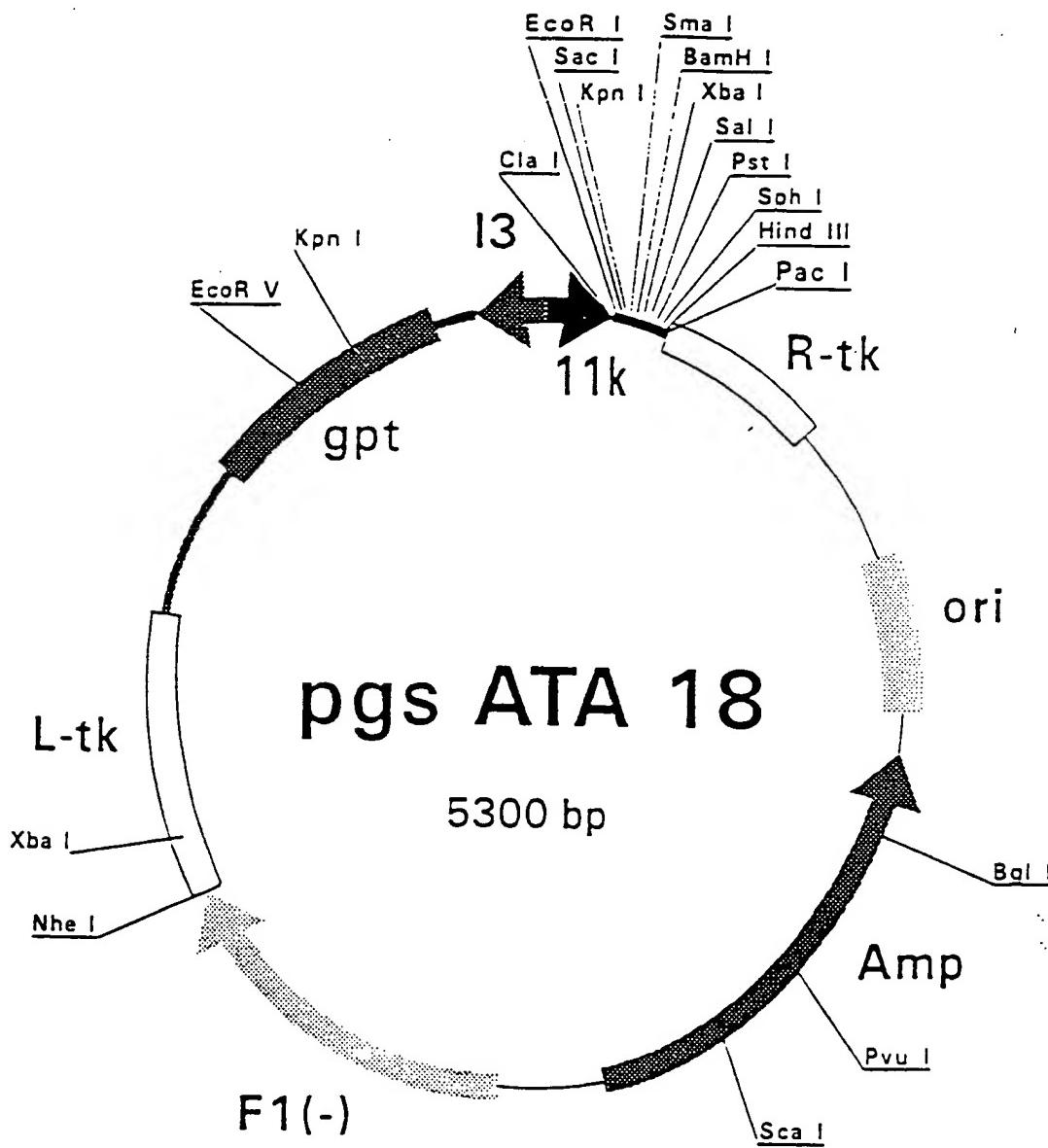


FIGURE 2

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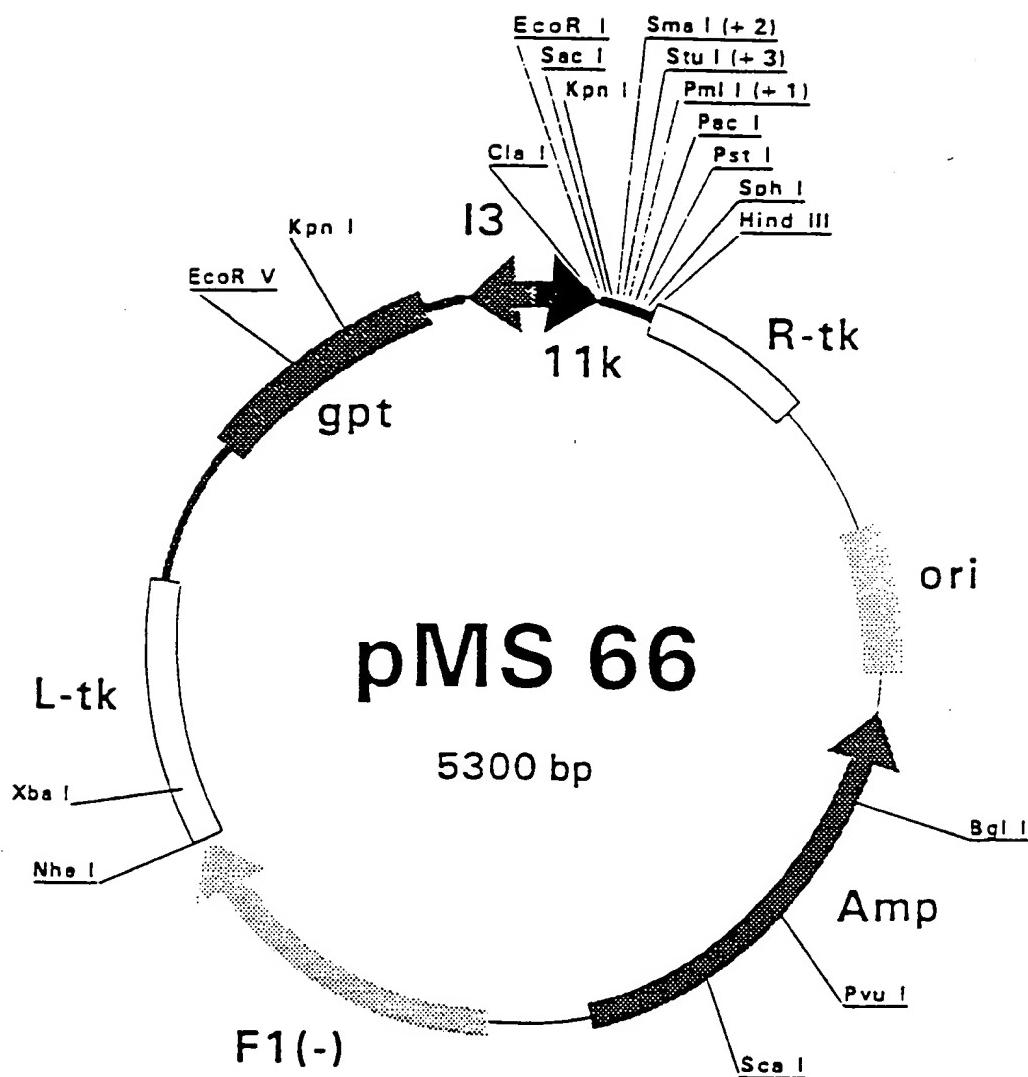


FIGURE 3

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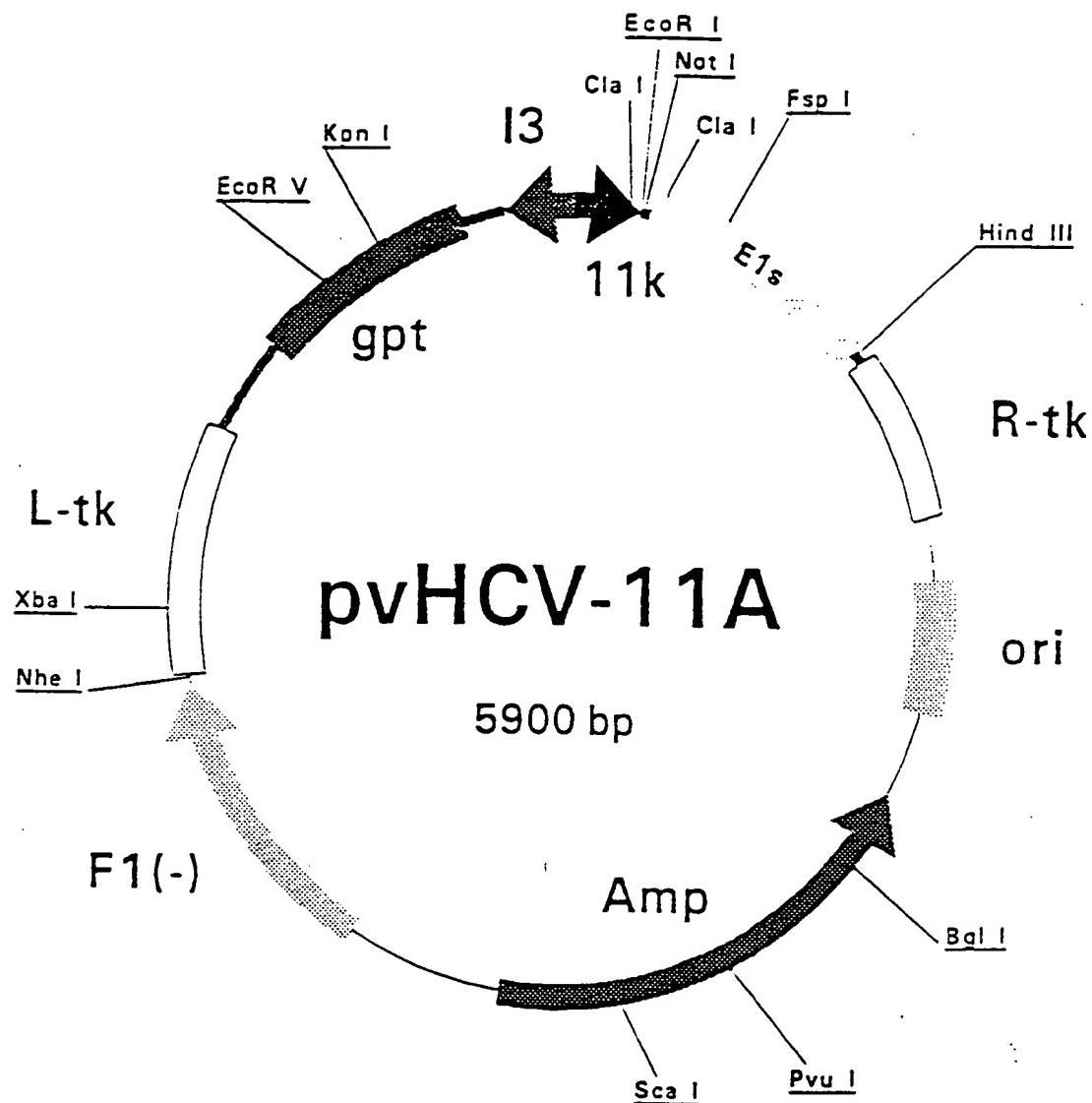


FIGURE 4

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## Anti-E1 levels in NON-responders to IFN treatment

Series 1

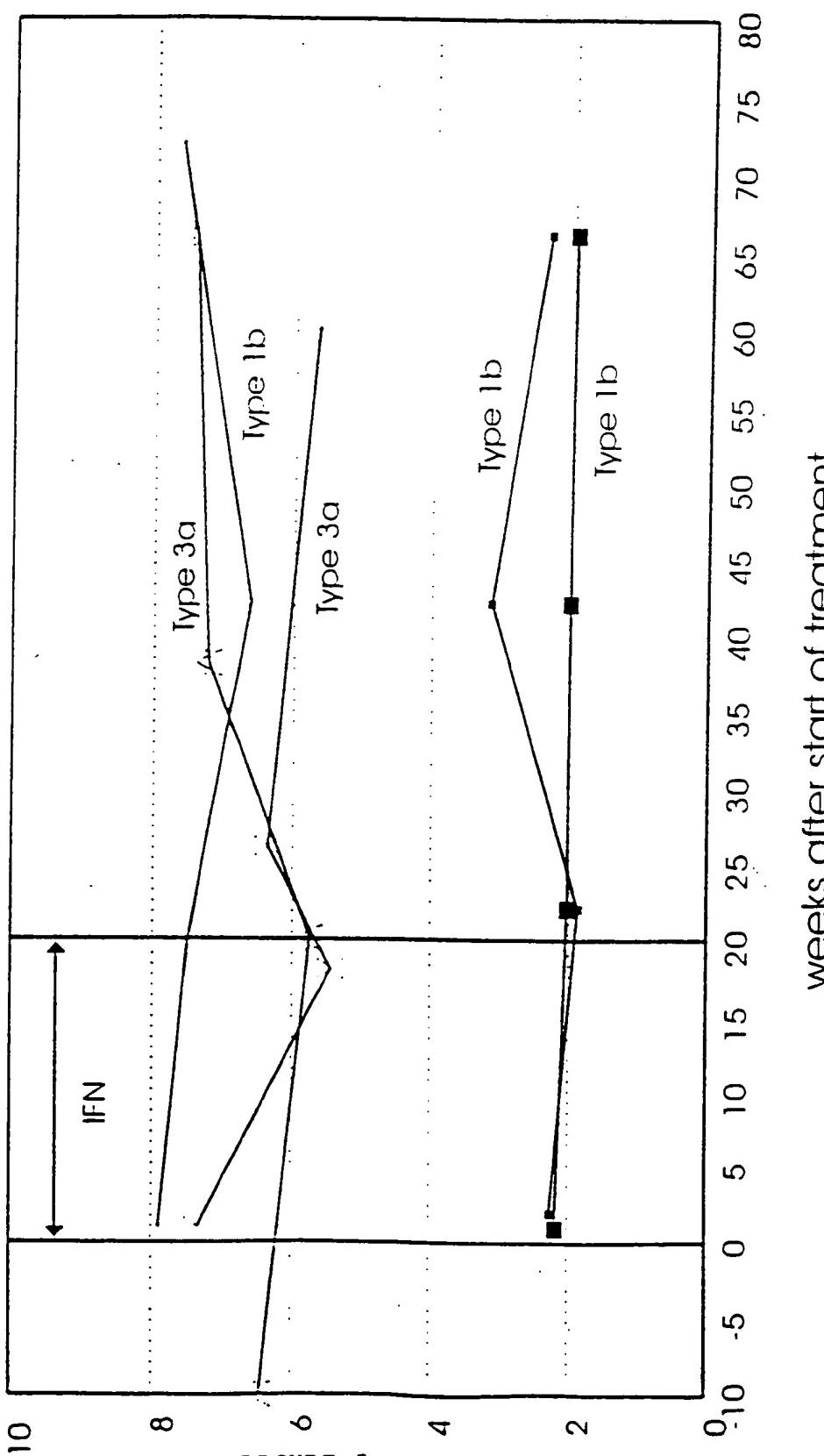


FIGURE 5

# Anti-E1 levels in RESPONDERS to IFN treatment

SERIES 1

S/N

12

10

8

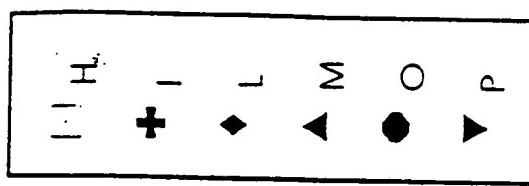
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4

2

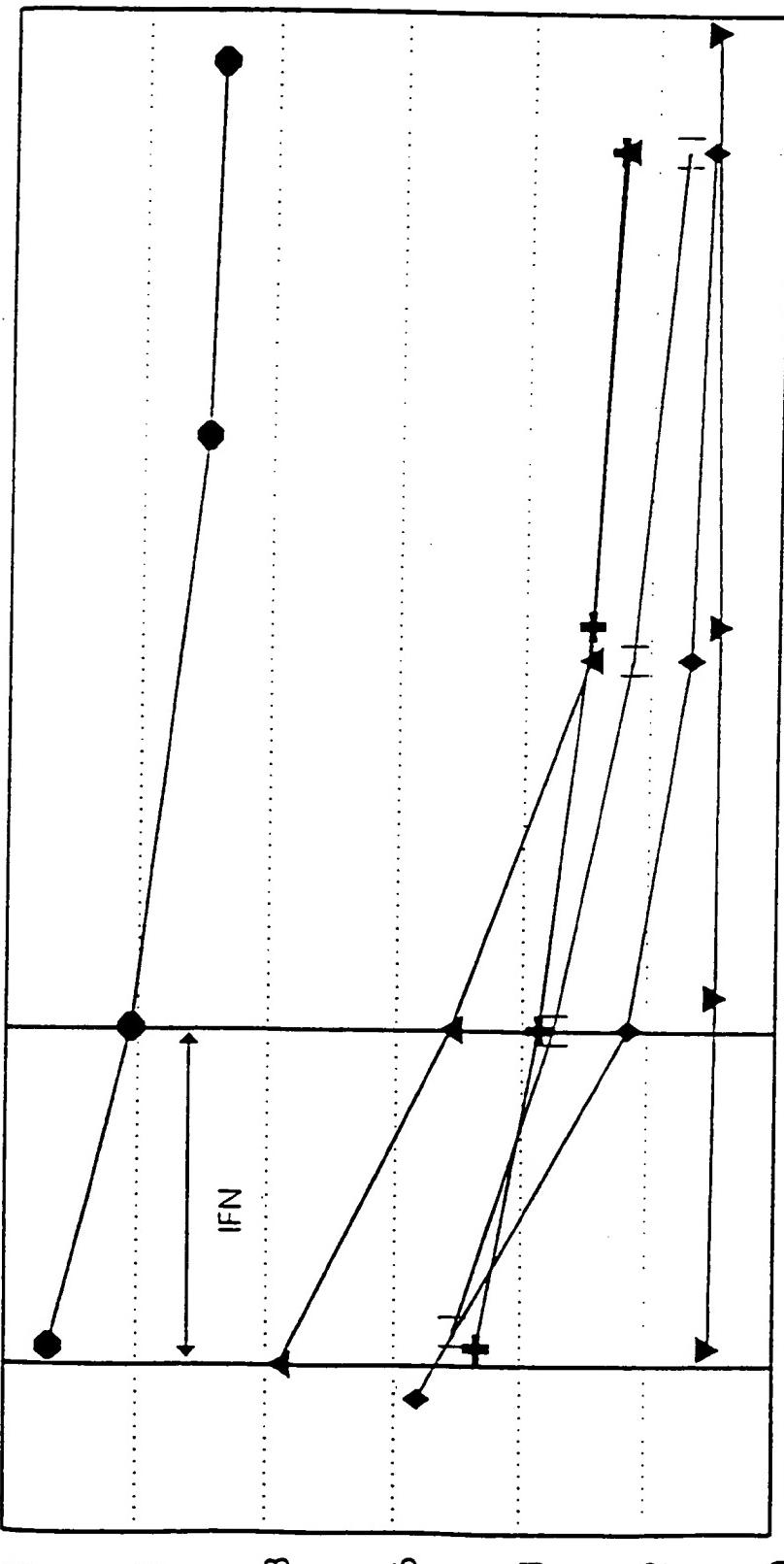
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weeks after start of treatment

0 10 20 30 40 50 60 70 80



## Anti-E1 levels in patients with COMPLETE response to IFN

SERIES 2

S/N

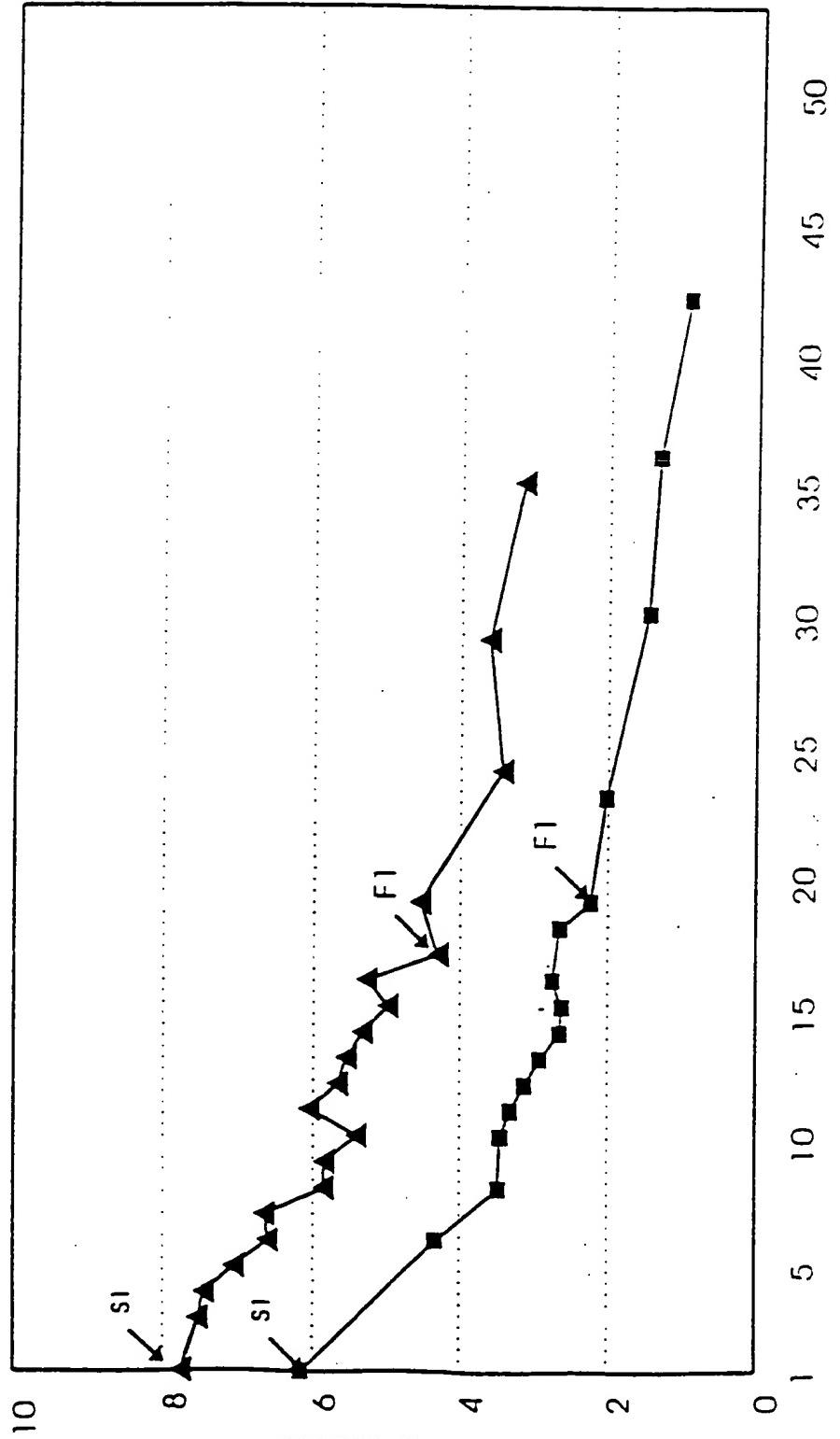
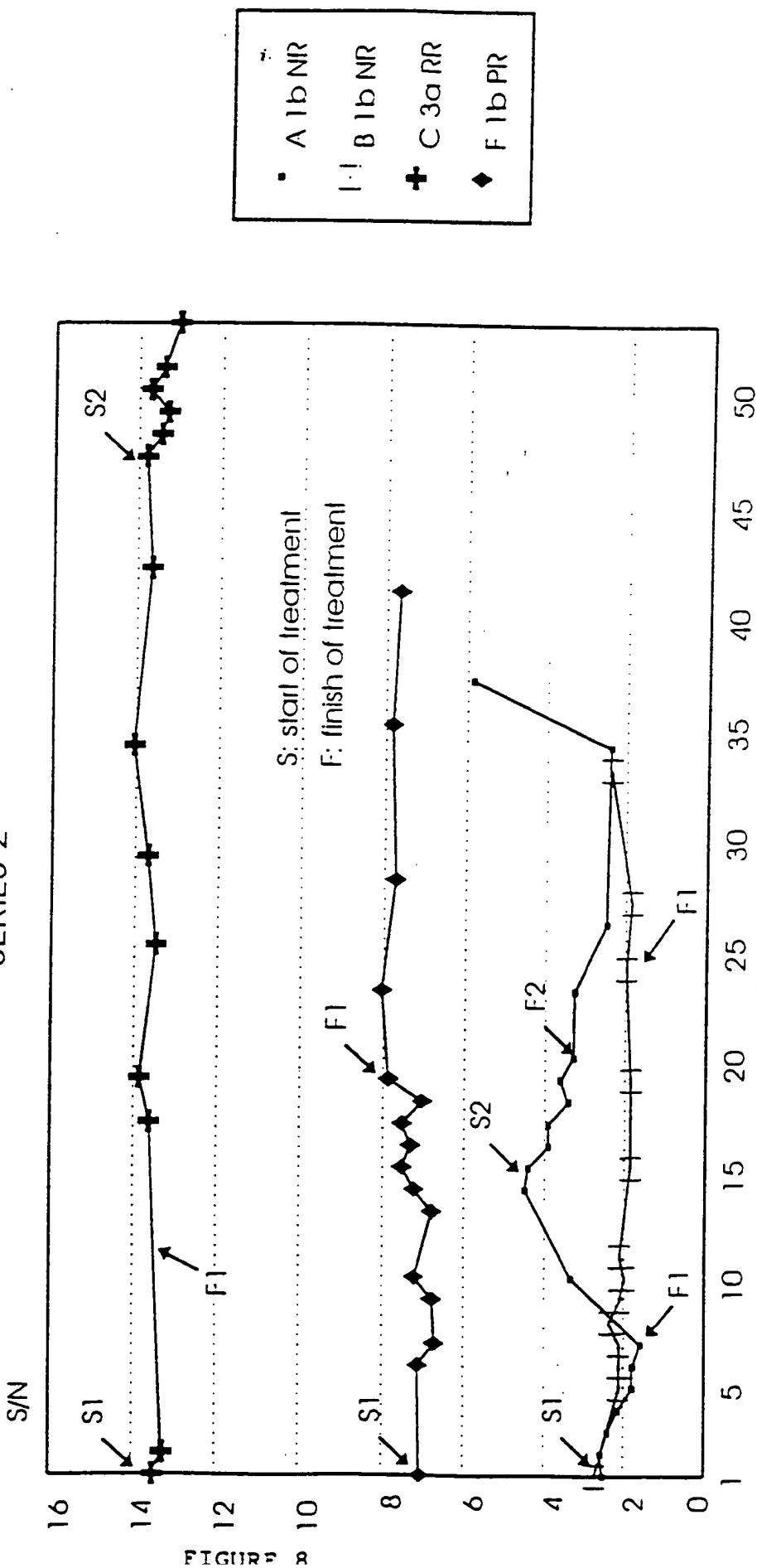


FIGURE 7

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# Anti-E1 levels in INCOMPLETE responders to IFN treatment

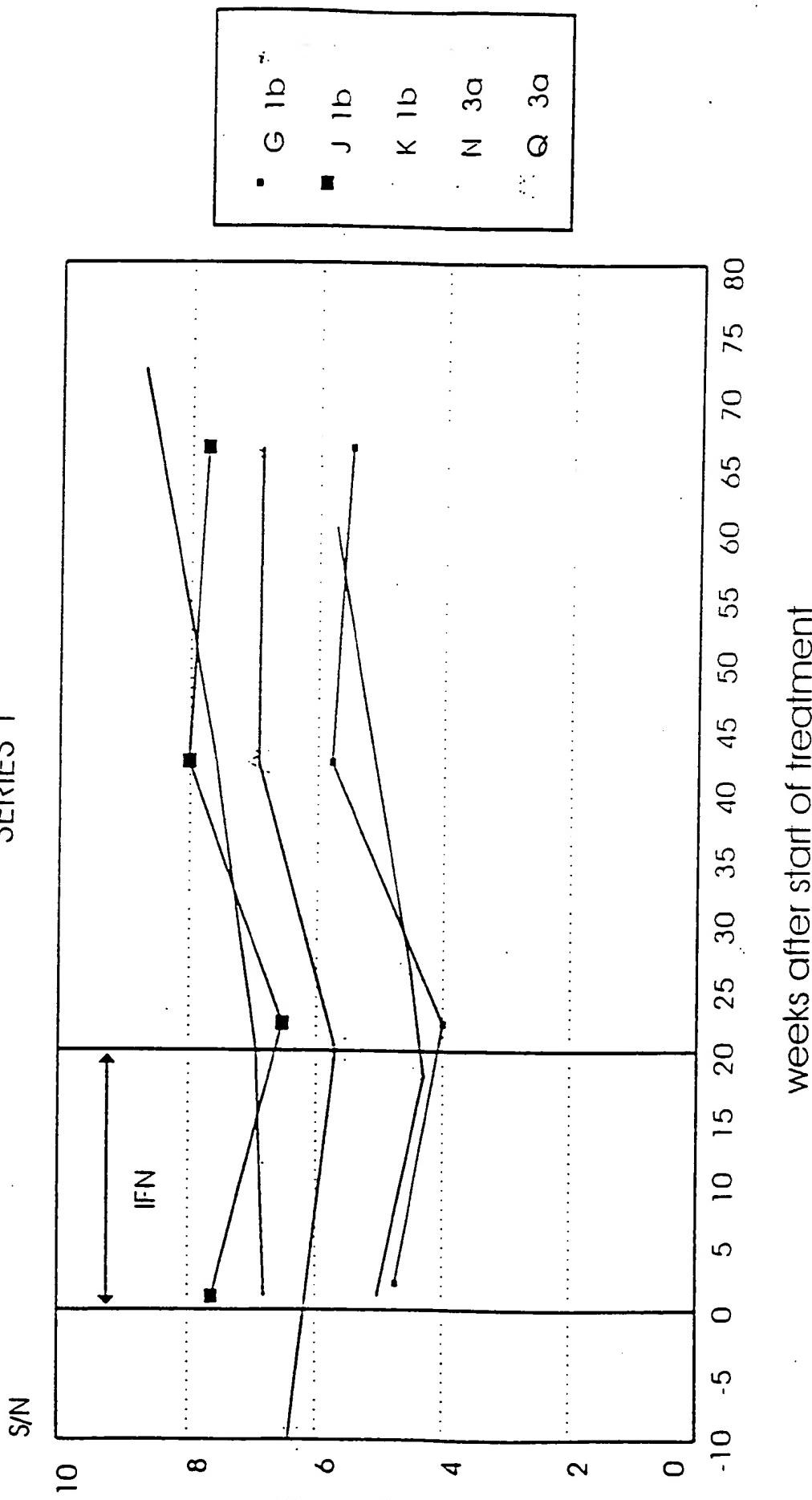
SERIES 2



months after start of treatment

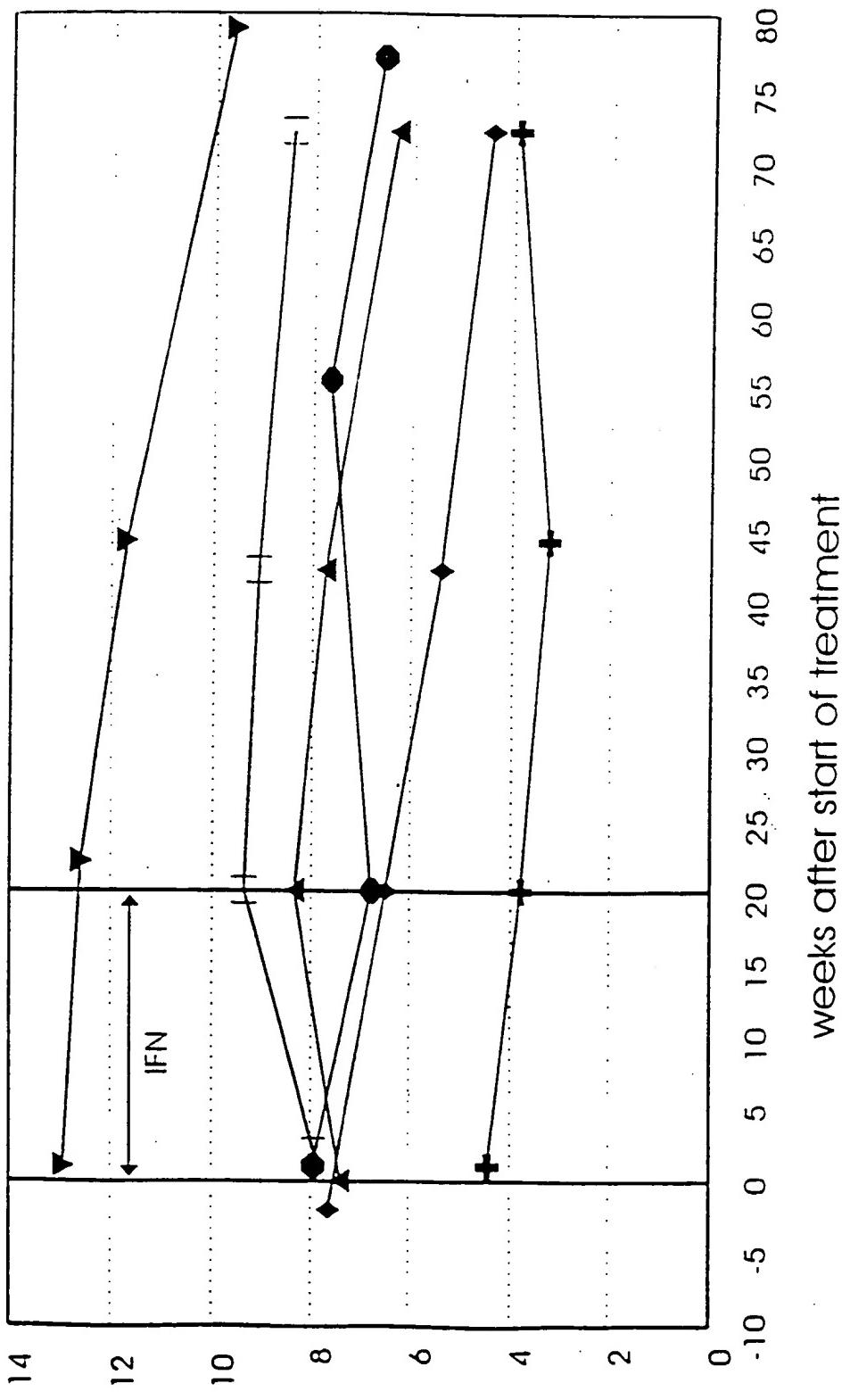
## Anti-E2 levels in NON-RESPONDERS to IFN treatment

SERIES 1



# Anti-E2 levels in RESPONDERS to IFN treatment

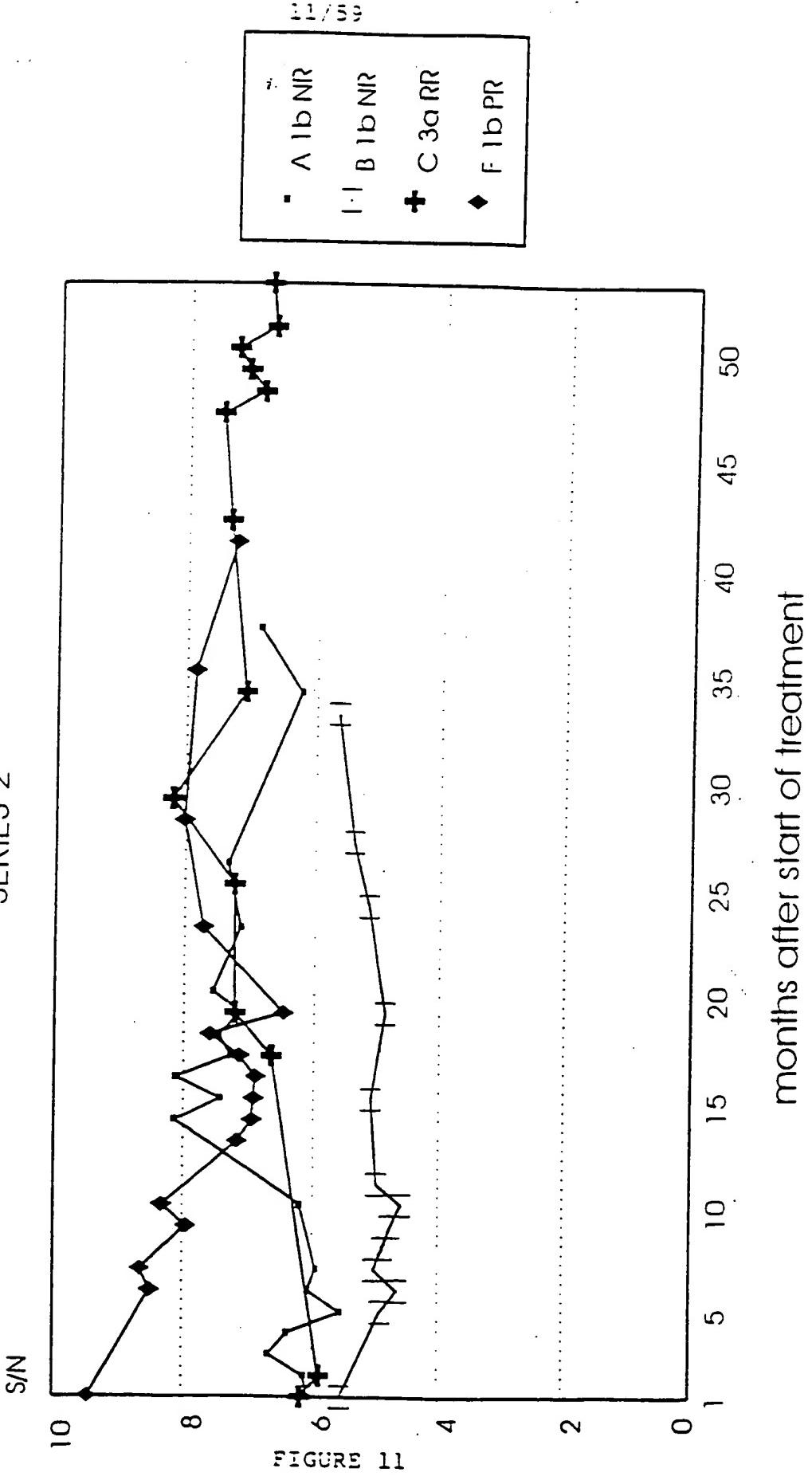
SERIES 1



weeks after start of treatment

# Anti-E2 levels in INCOMPLETE responders to IFN treatment

SERIES 2



WO 96/04385

PCT/EP95/03031

## Anti-E2 levels in COMPLETE responders to IFN treatment

SERIES 2

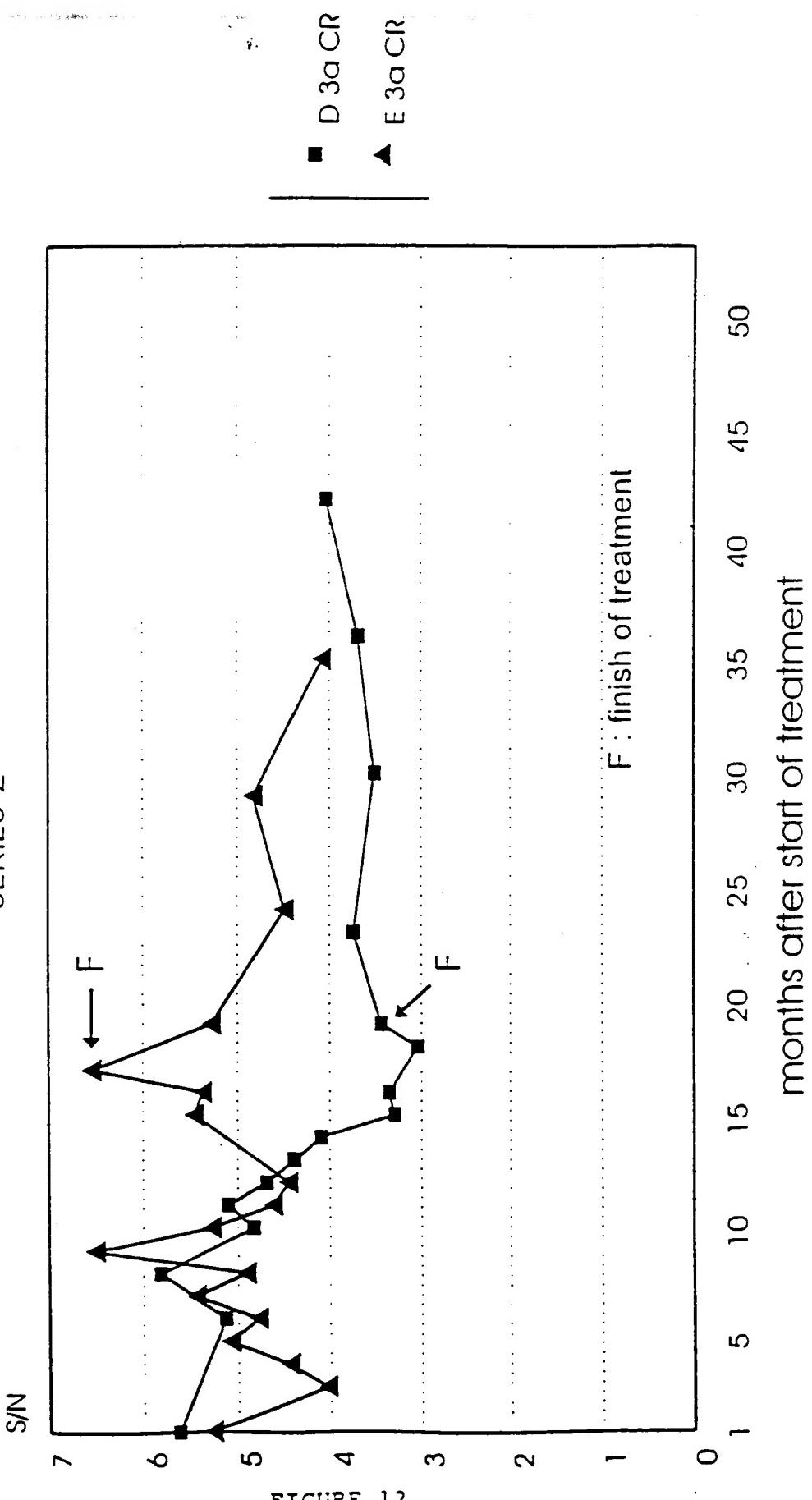
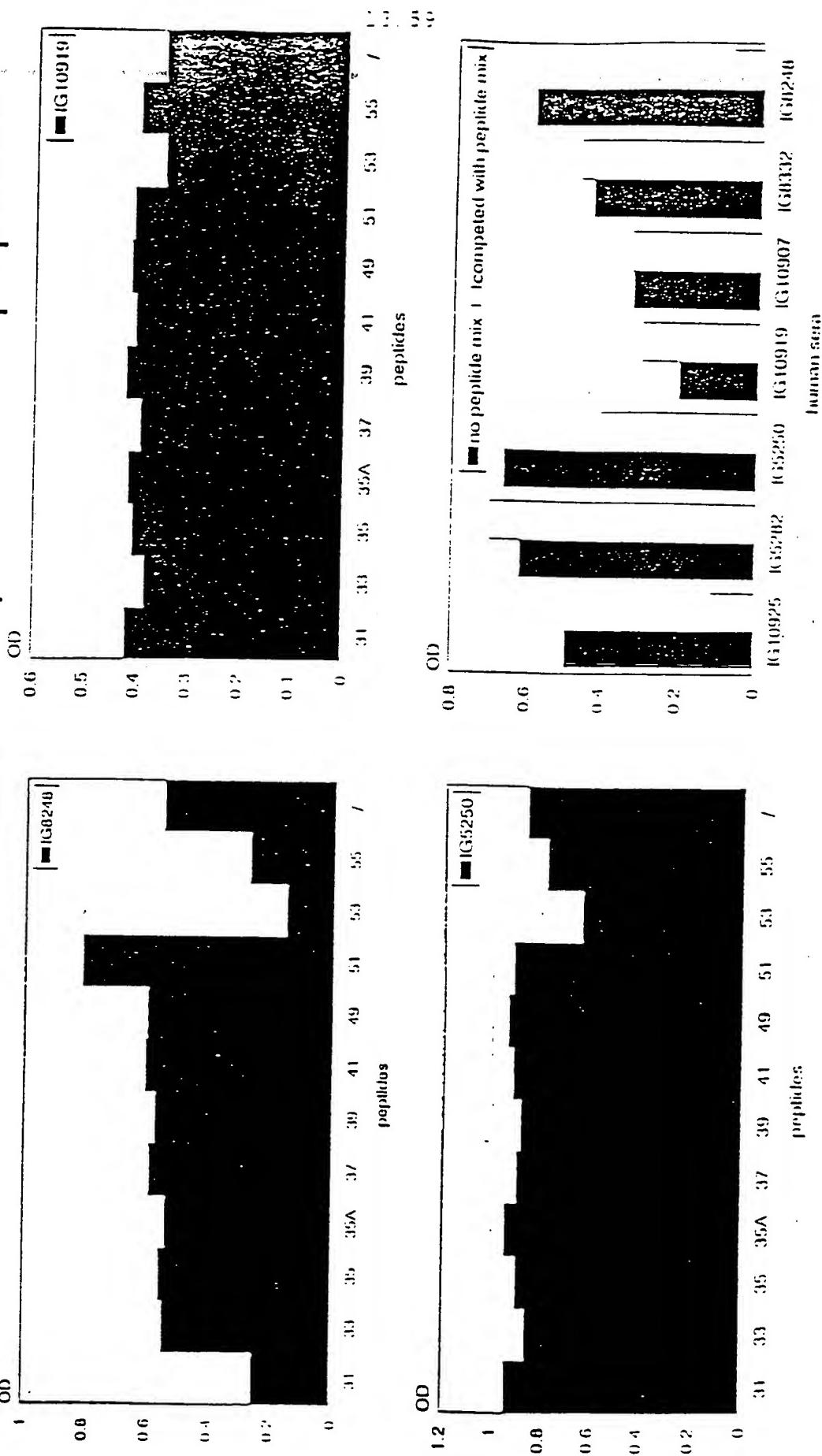


FIGURE 1

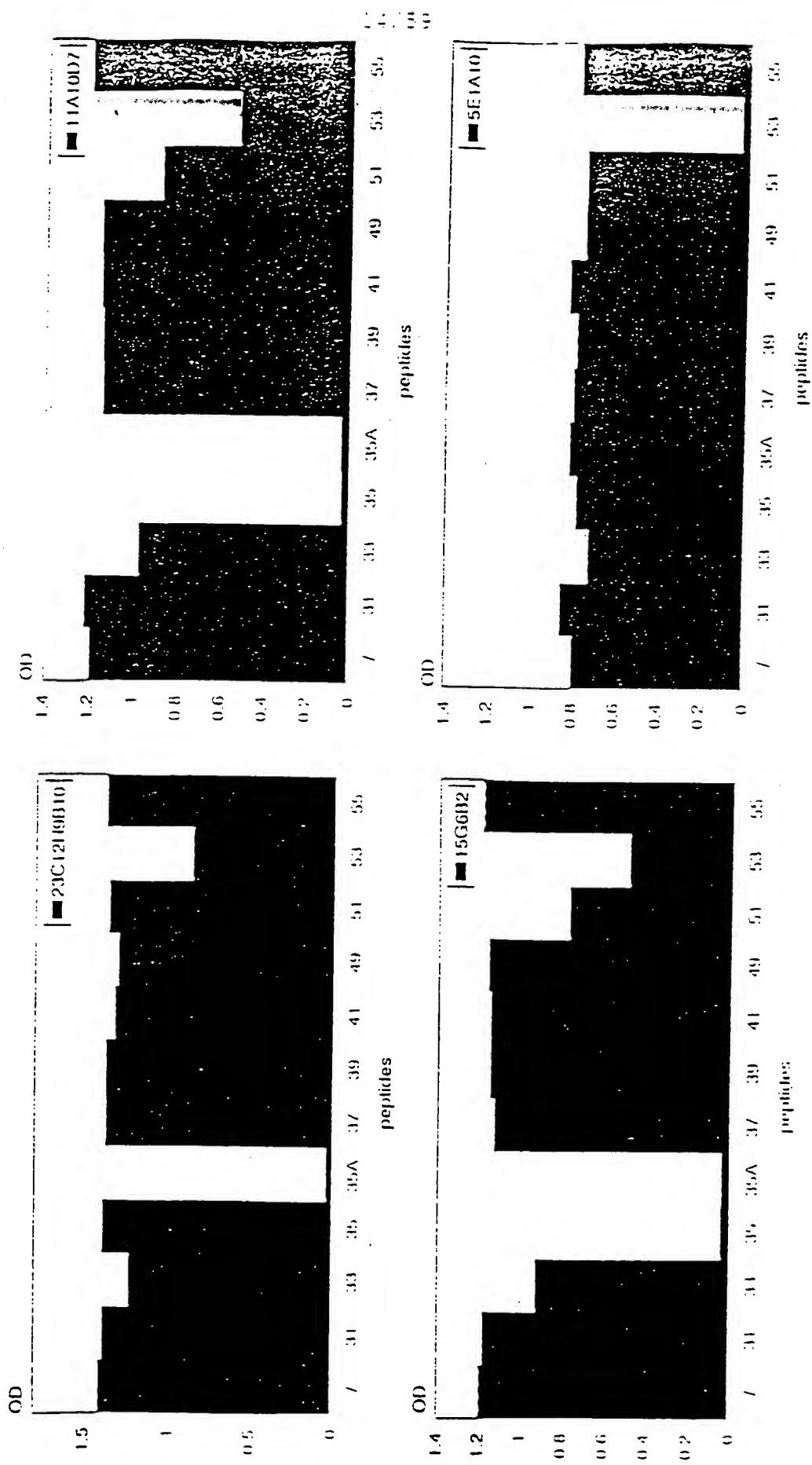
# FIGURE 13

## Human anti-E1 reactivity competed with peptides



# FIGURE 14.

Competition of reactivity of anti-E1 Mabs with peptides



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# Anti-E1 (epitope 1) levels in NON-RESPONDERS to IFN treatment

## SERIES 1

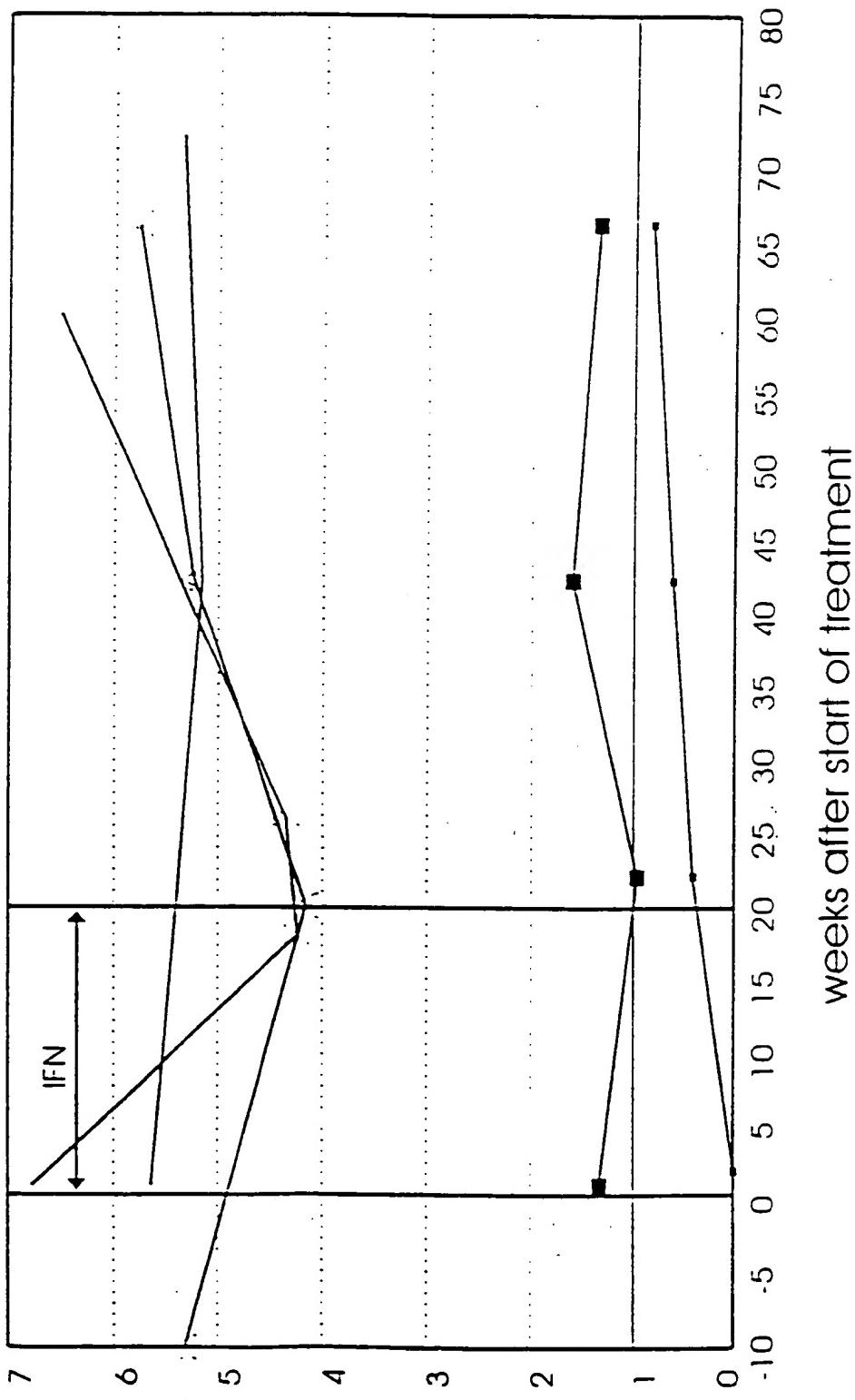


FIGURE 15

# Anti-E1 (epitope 1) levels in RESPONDERS to IFN treatment

SERIES 1

S/N

10

8

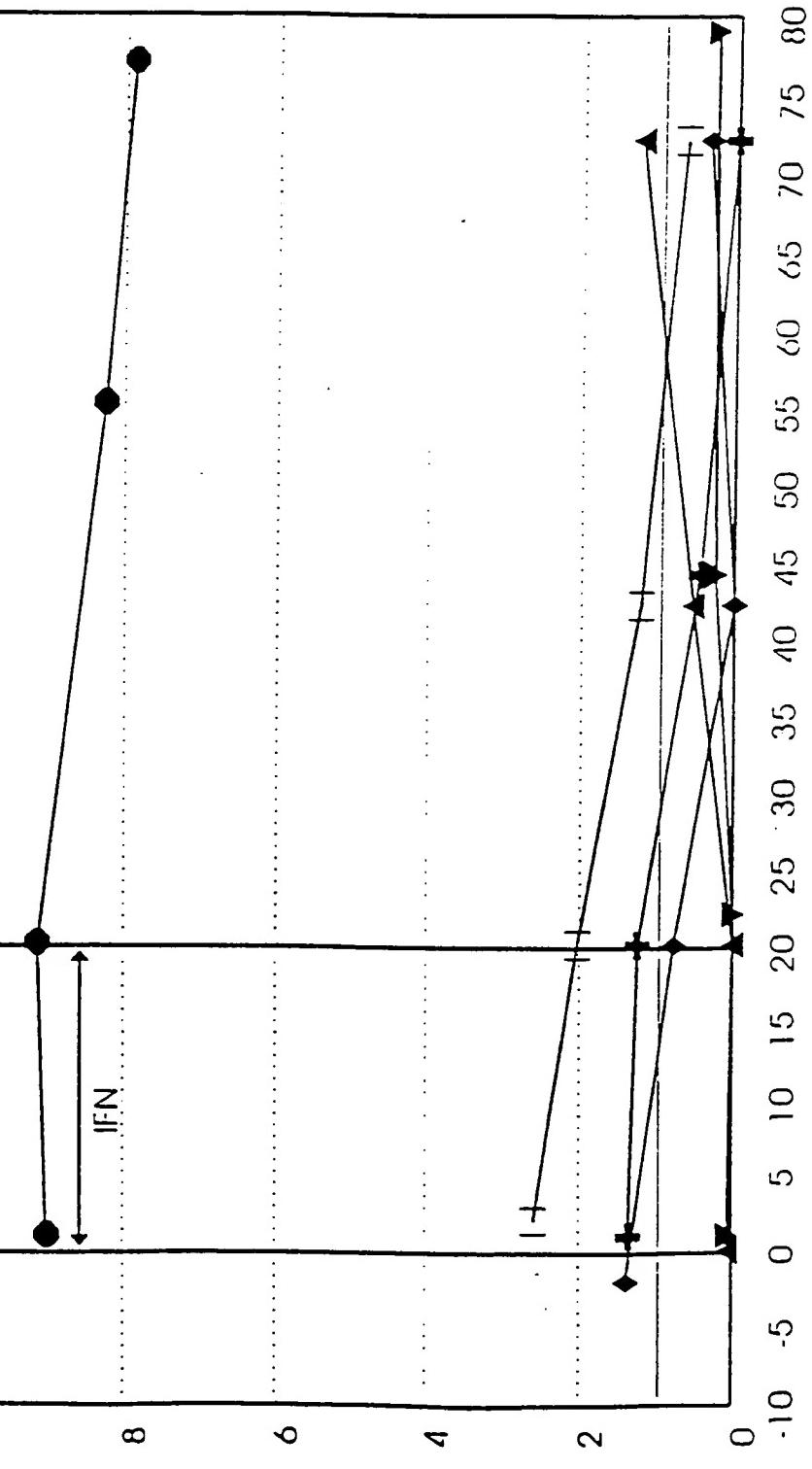
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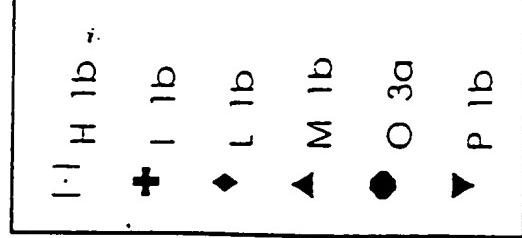
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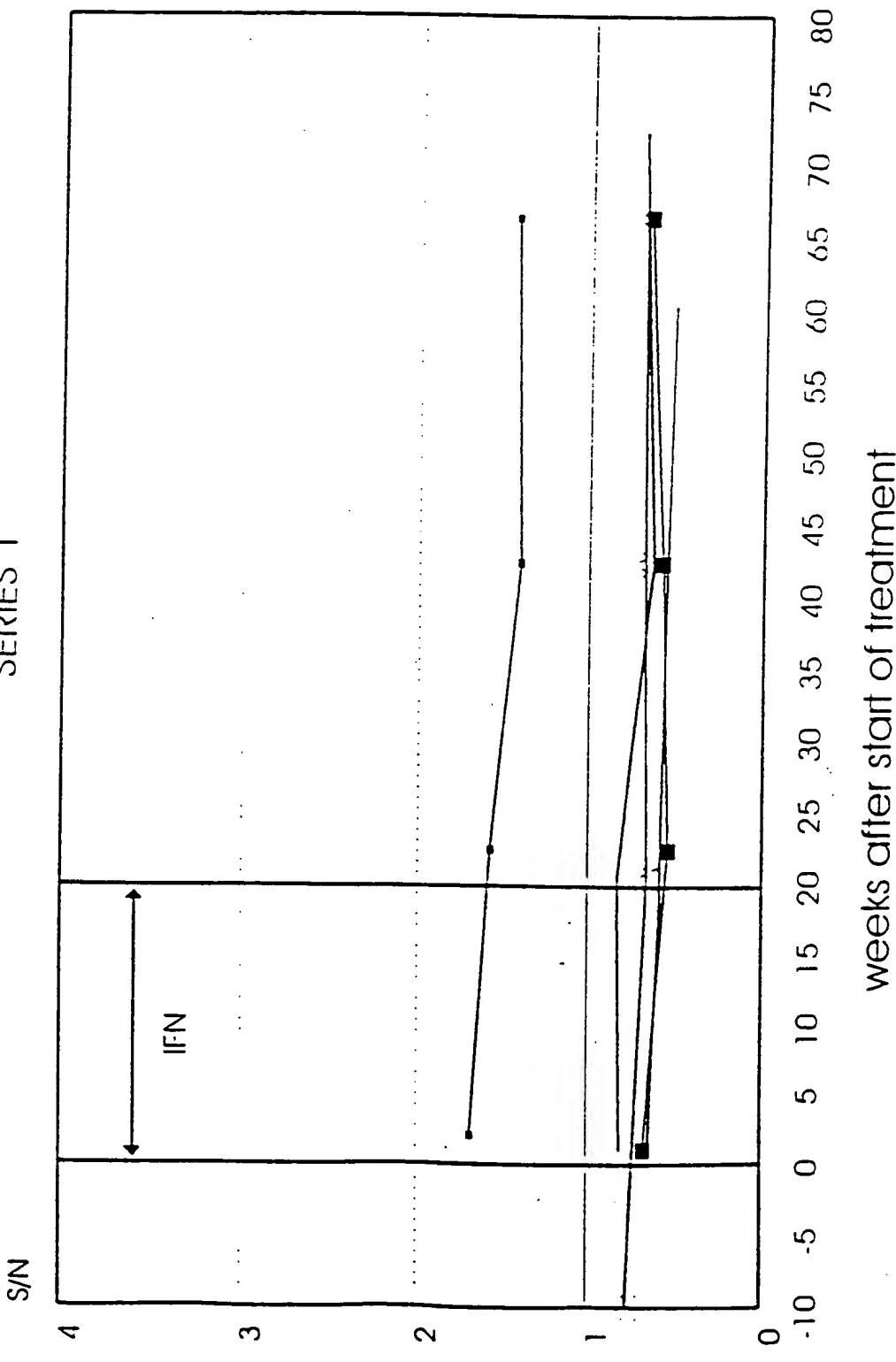


weeks after start of treatment



**anti-E1 (epitope 2) levels in NON-RESPONDERS to IFN treatment**

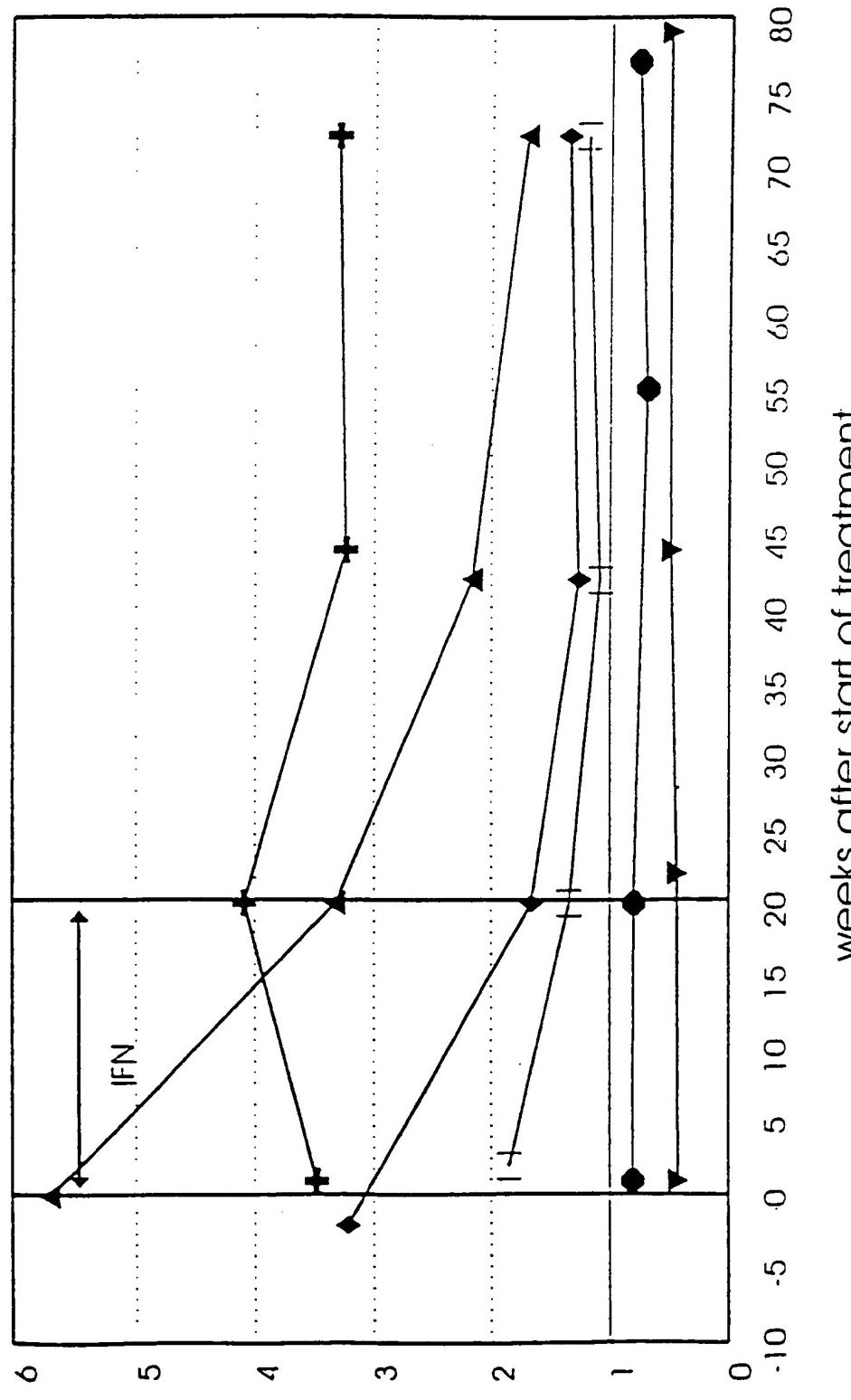
**SERIES 1**



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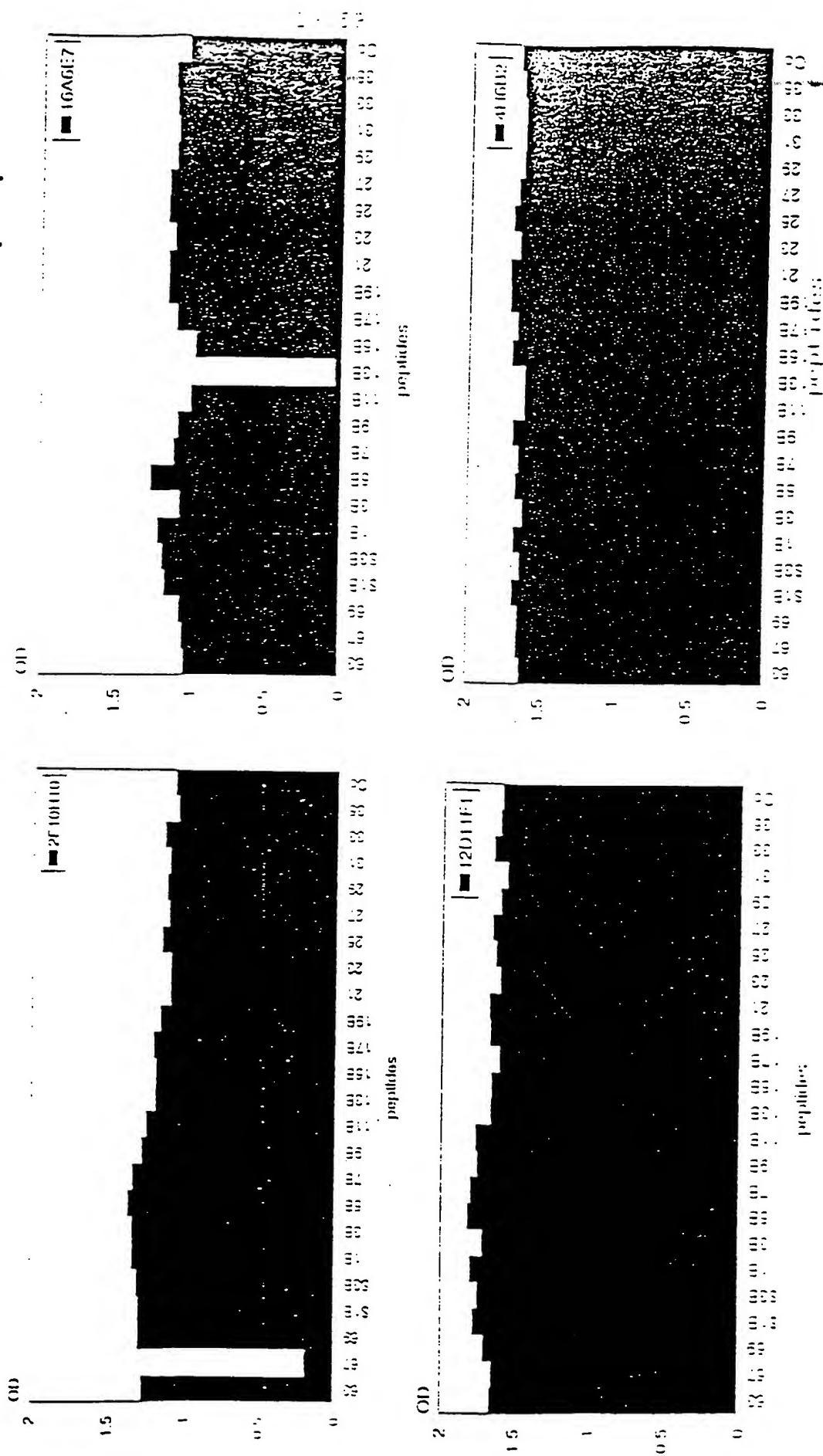
## Anti-E1 (epitope 2) levels in RESPONDERS to IFN treatment

SERIES 1



# FIGURE 19

Competition of reactivity of anti-E2 Mabs with peptides



**FIGURE 20**  
Human anti-E2 reactivity competed with peptides

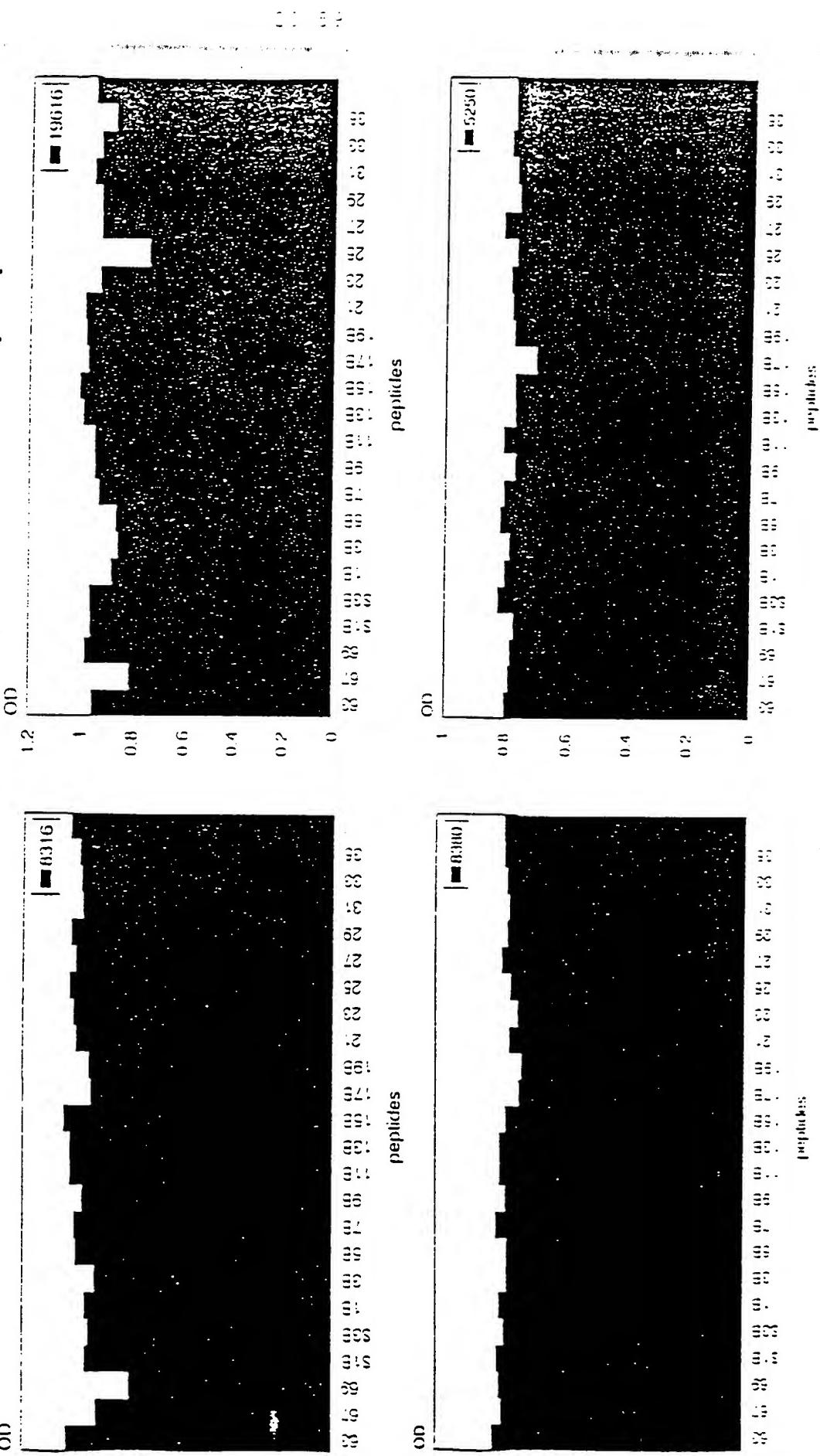


Figure 21

5' GGCATGCAAGCTTAATTAAATT3' (SEQ ID NO 1)  
3'ACGTCCGTACGTTCGAATTAAATTAAATCGA5' (SEQ ID NO 94)

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TAATTAACTGCA 3' (SEQ ID NO 2)  
3'CCTCCGGACGTGCACTAGCTCCCGTCTGGTAGTGGTAGTGATTATCAATTAAATTG  
5' (SEQ ID NO 95)

## SEQ ID NO 3 (HCCI9A)

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CCAACCTCAAGCATTGTGTATGAGGCAGCGGACATGATCATGCACACCCCCGGTGCCT  
GCCCTGCGTTCGGAGAACAACTCTCCCGCTGCTGGTAGCGCTCACCCCCACGCTC  
GCAGCTAGGAACGCCAGCGTCCCCACCGACAATACGACGCCACGTCGATTTGCTCG  
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CTCGTCTCCCAGCTGTTACCATCTCGCCTGCCGGCATGAGACGGTGCAGGACTGCA  
ATTGCTCAATCTATCCCGGCCACATAACAGGTCAACCGTATGGCTTGGGATATGATGAT  
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## SEQ ID NO 5 (HCCI10A)

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TTCCGCTATGTACGTGGGGACCTCTCGGGATCTGCTTCCCTCGTCTCCCAGCTGTTCA  
CCATCTCGCCTGCCGGCATGAGACGGTGAGGACTGCAATTGCTCAATCTATCCCGG  
CCACATAACGGGTACCGTATGGCTGGATATGATGATGAACGGTCGCCTACAACG  
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## SEQ ID NO 7 (HCCI11A)

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## SEQ ID NO 11 (HCCI13A)

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## SEQ ID NO 13 (HCC117A)

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## SEQ ID NO 15 (HCPr51)

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## SEQ ID NO 16 (HCPr52)

ATGTTGGGTAAAGGTATCGATAACCCT

## SEQ ID NO 17 (HCPr53)

CTATTAGGACCAAGTTCATCATCATATCCCA

## SEQ ID NO 18 (HCPr54)

CTATTACCAAGTTCATCATCATATCCCA

## SEQ ID NO 19 (HCPr107)

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## SEQ ID NO 35 (HCCL22A)

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## SEQ ID NO 39 (HCCI42)

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AGGGTTCTTGCCGCACTATTCTACAAACACAAATTCAACTCGTCTGGATGCCAGAG  
CGCTTGGCCAGCTGCGCTCCATCGACAAGTTGCTCAGGGTGGGTCCCCTCACTT  
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CTGTTGTGGTGGGACGACCGATCGGTTGGTGTCCCCACGTATAACTGGGGGGCGAA  
CGACTCGGATGTGCTGATTCTAACAAACACGCGGCCGCCGAGGCAACTGGTCGGC  
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TCGGGGGGGCCGGCAACAAACACCTTGACCTGCCCCACTGACTGTTTCGGAAGCACCC  
CGAGGCCACCTACGCCAGATCGGTTCTGGCCCTGGCTGACACCTAGGTGTATGGTT  
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SEQ ID NO 41 (HCCI43)

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TCGGACCAGAGGCCCTACTGCTGGCACTACGCGCTCGACCGTGTGGTATTGACCCG  
CGTCTCAGGTGTGCGGTCCAGTGTATTGCTTACCCCGAGCCCTGTTGTGGTGGGAC  
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CTCTGGCACTACCCCTGCACTGTCAACTTCAACCATCTCAAGGTTAGGATGTACGTGG  
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## SEQ ID NO 43 (HCCI44)

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GACCGATCGGTTGGTGTCCCCACGTATAACTGGGGGCGAACGACTCGGATGTGCTG  
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CAGATGCCGTTCTGGCCCTGGCTGACACCTAGGTGTATGGTTCAACATACCGATATAGG  
CTCTGGCACTACCCCTGCACTGTCAACTTCAACATCTTCAAGGTTAGGATGTACGTGGG  
GGCGTGGAGCACAGGTTCGAAGCCGATGCAATTGGACTCGAGGAGAGCGTTGTGA  
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## SEQ ID NO 45 (HCCL64)

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## SEQ ID NO 47 (HCCI65)

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CCCCACGTATAACTGGGGGGGAACGACTCGGATGTGCTGATTCTCAACAAACACGCGG  
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## SEQ ID NO 49 (HCCI66)

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CTCGTGGGAGGCAGAACCTATCCCCAAGGCTGCCGACCCGAGGGTAGGGCCTGGG  
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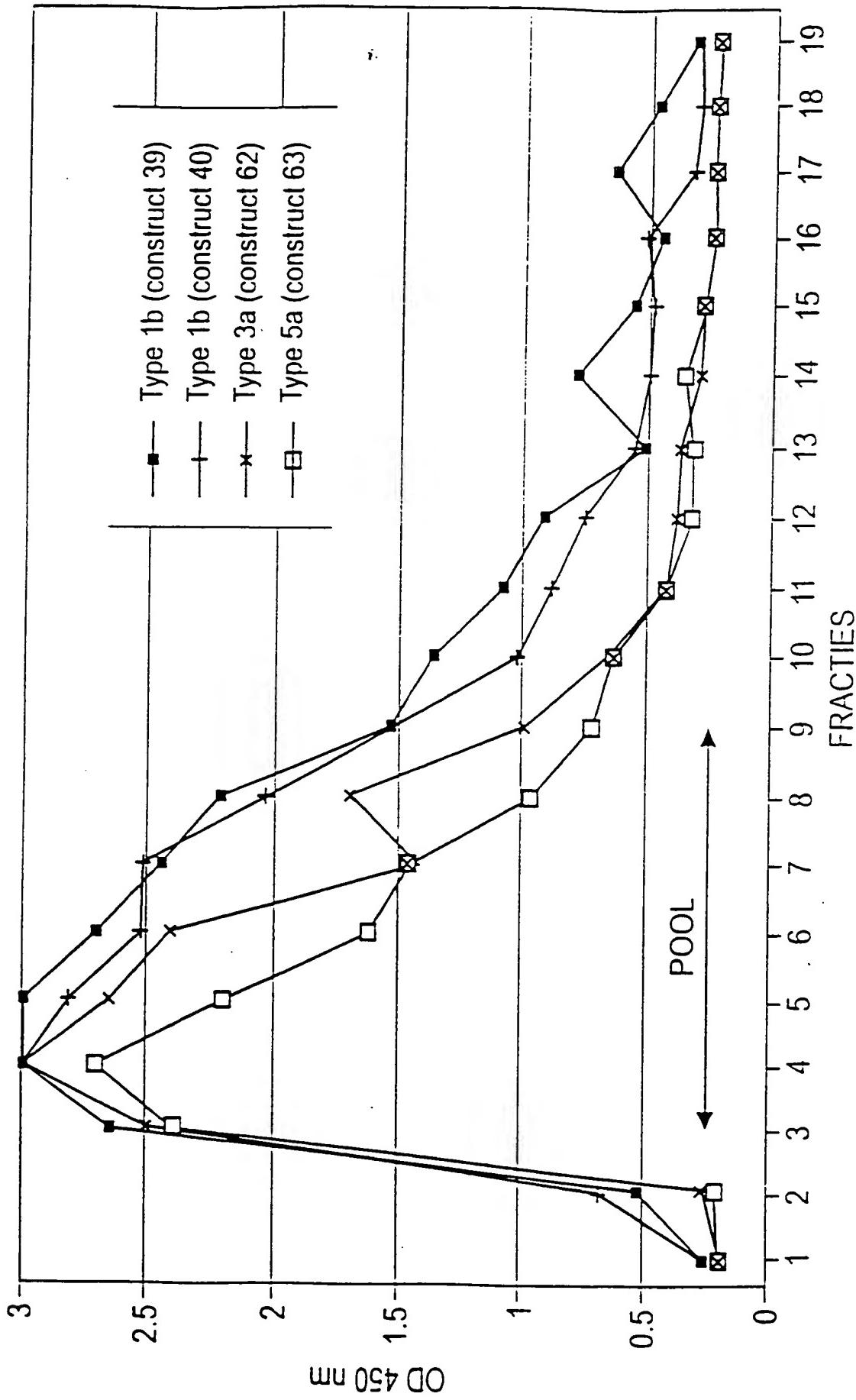
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Figure 22

OD measured at 450 nm  
construct

Fraction	volume	dilution	39 Type 1b	40 Type 1b	62 Type 3a	63 Type 5a
START	23 ml	1/20	2.517	1.954	1.426	1.142
FLOW THROUGH	23 ml	1/20	0.087	0.085	0.176	0.120
1	0.4 ml	1/200	0.102	0.051	0.048	0.050
2			0.395	0.550	0.090	0.067
3			2.627	2.603	2.481	2.372
4			3	2.967	3	2.694
5			3	2.810	2.640	2.154
6			2.694	2.499	1.359	1.561
7			2.403	2.481	0.347	1.390
8			2.176	1.970	1.624	0.865
9			1.461	1.422	0.887	0.604
10			1.286	0.926	0.543	0.519
11			0.981	0.781	0.294	0.294
12			0.812	0.650	0.249	0.199
13			0.373	0.432	0.239	0.209
14			0.653	0.371	0.145	0.184
15			0.441	0.348	0.151	0.151
16			0.321	0.374	0.098	0.106
17			0.525	0.186	0.099	0.108
18			0.351	0.171	0.083	0.090
19			0.192	0.164	0.084	0.087

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## 35/59 Figure 24

Fraction	volume	dilution	OD measured at 450 nm			
			construct			
			39 Type 1b	40 Type 1b	62 Type 3a	63 Type 5a
20	250 $\mu$ l	1/200	0.072	0.130	0.096	0.051
21			0.109	0.293	0.084	0.052
22			0.279	0.249	0.172	0.052
23			0.093	0.151	0.297	0.054
24			0.080	0.266	0.438	0.056
25			0.251	0.100	0.457	0.048
26			3	1.649	0.722	0.066
27			3	3	2.528	0.889
28			3	3	3	2.345
29			3	3	2.849	2.580
30			2.227	1.921	1.424	1.333
31			0.263	0.415	0.356	0.162
32			0.071	0.172	0.154	0.064
33			0.103	0.054	0.096	0.057
34			0.045	0.045	0.044	0.051
35			0.043	0.047	0.045	0.046
36			0.045	0.045	0.049	0.040
37			0.045	0.047	0.046	0.048
38			0.046	0.048	0.047	0.057
39			0.045	0.048	0.050	0.057
40			0.046	0.049	0.048	0.049

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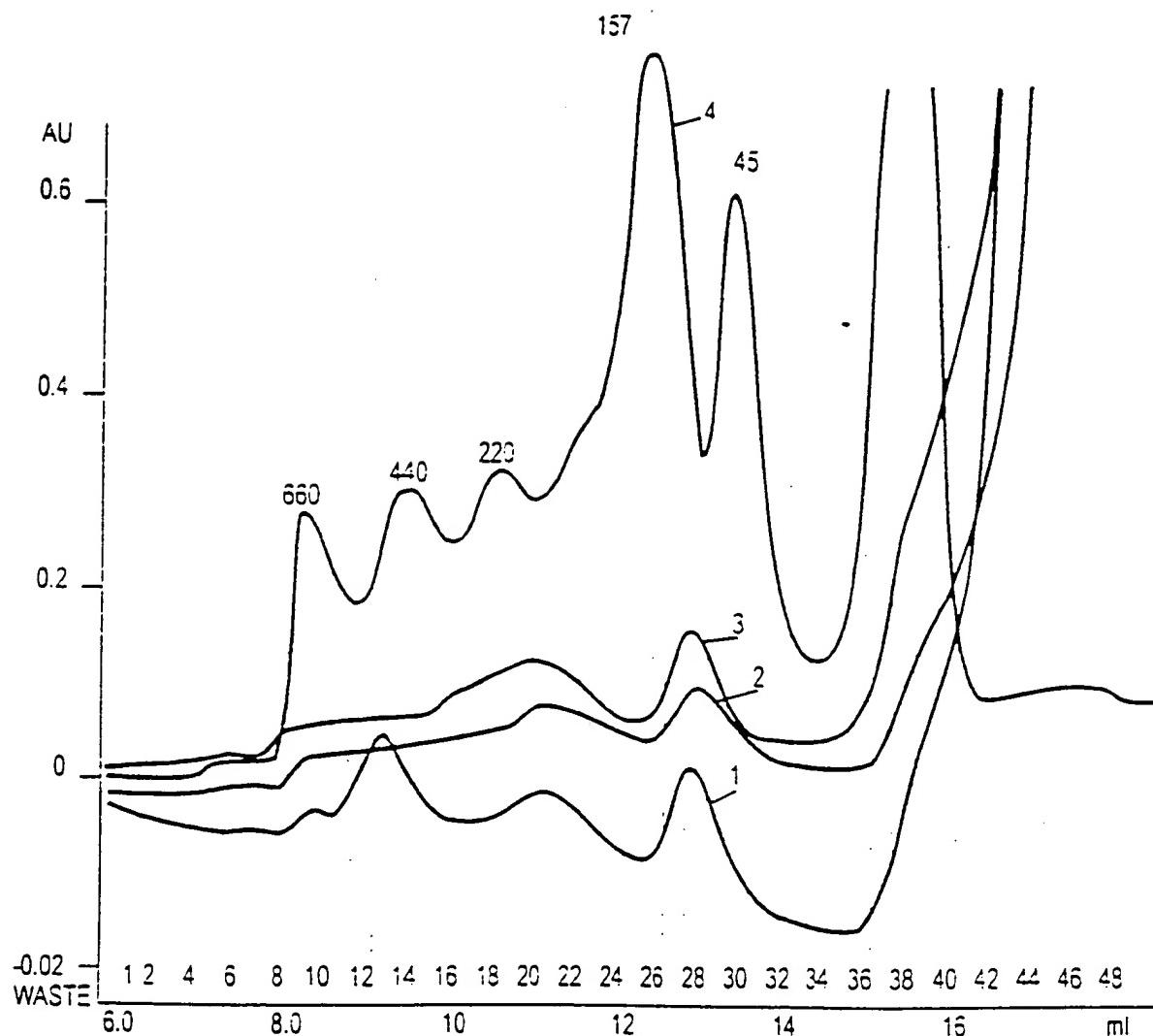


FIGURE 25

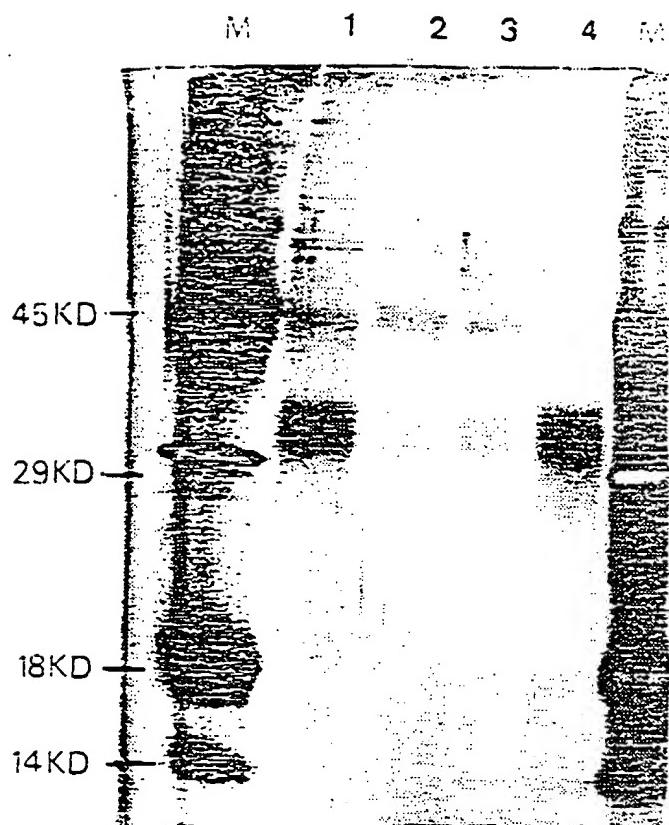


Figure 26

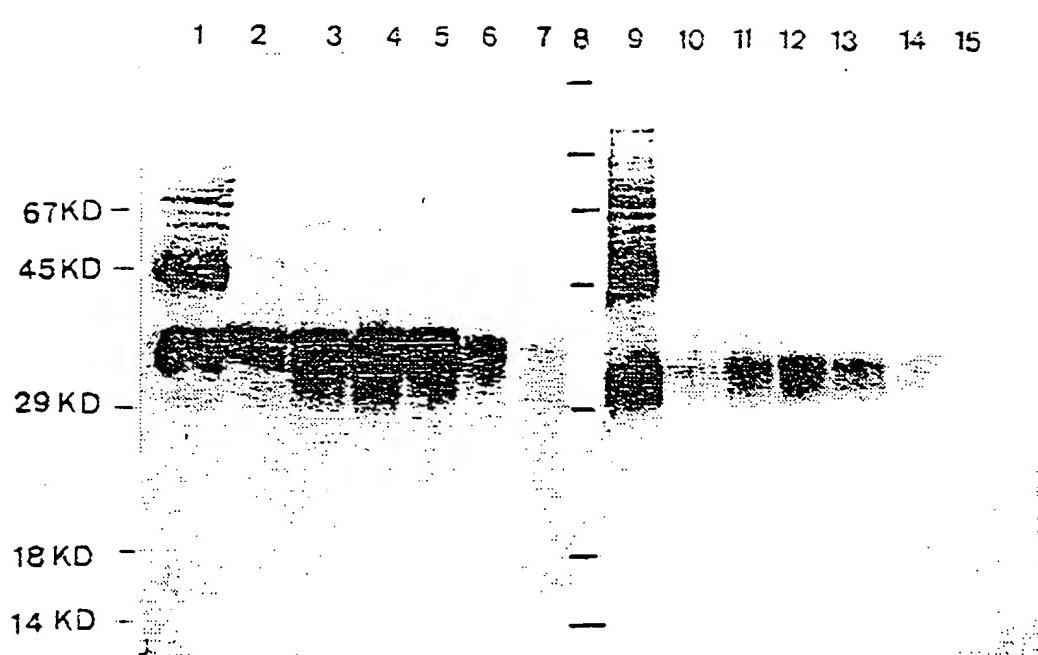


Figure 27

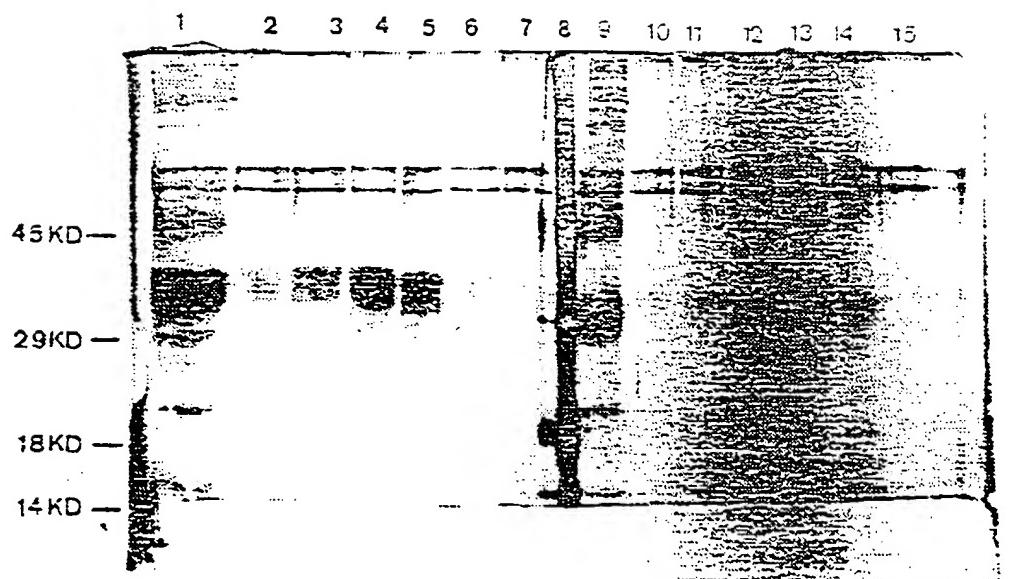


Figure 28

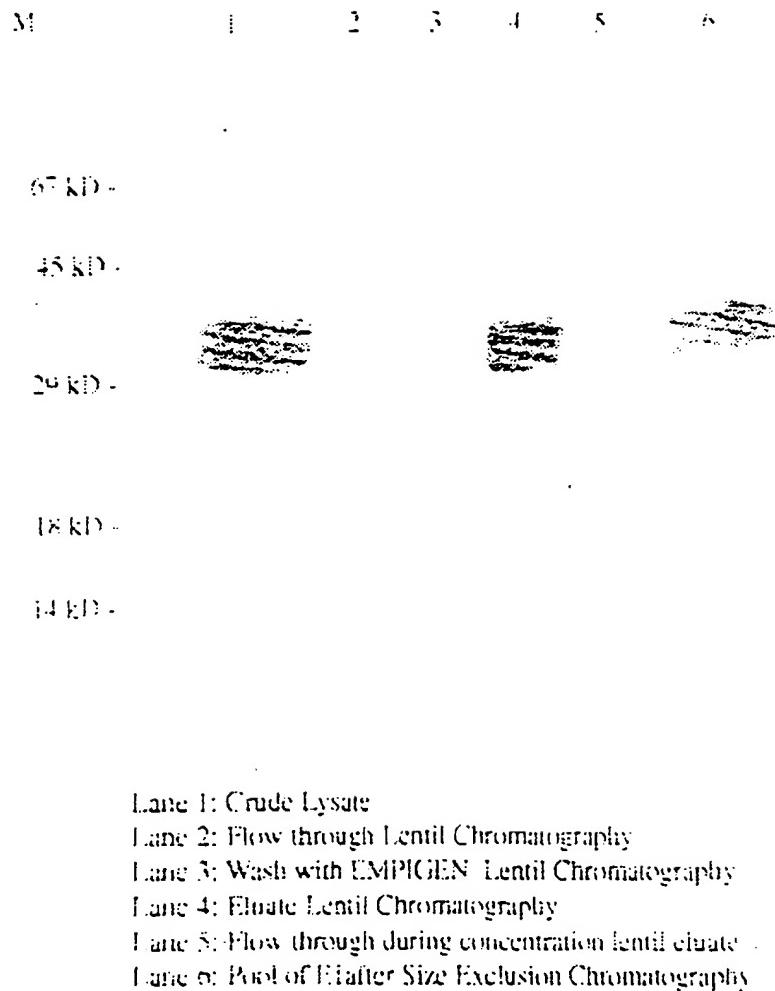


Figure 29: Western Blot Analysis with anti-E1 mouse monoclonal 5E1A10

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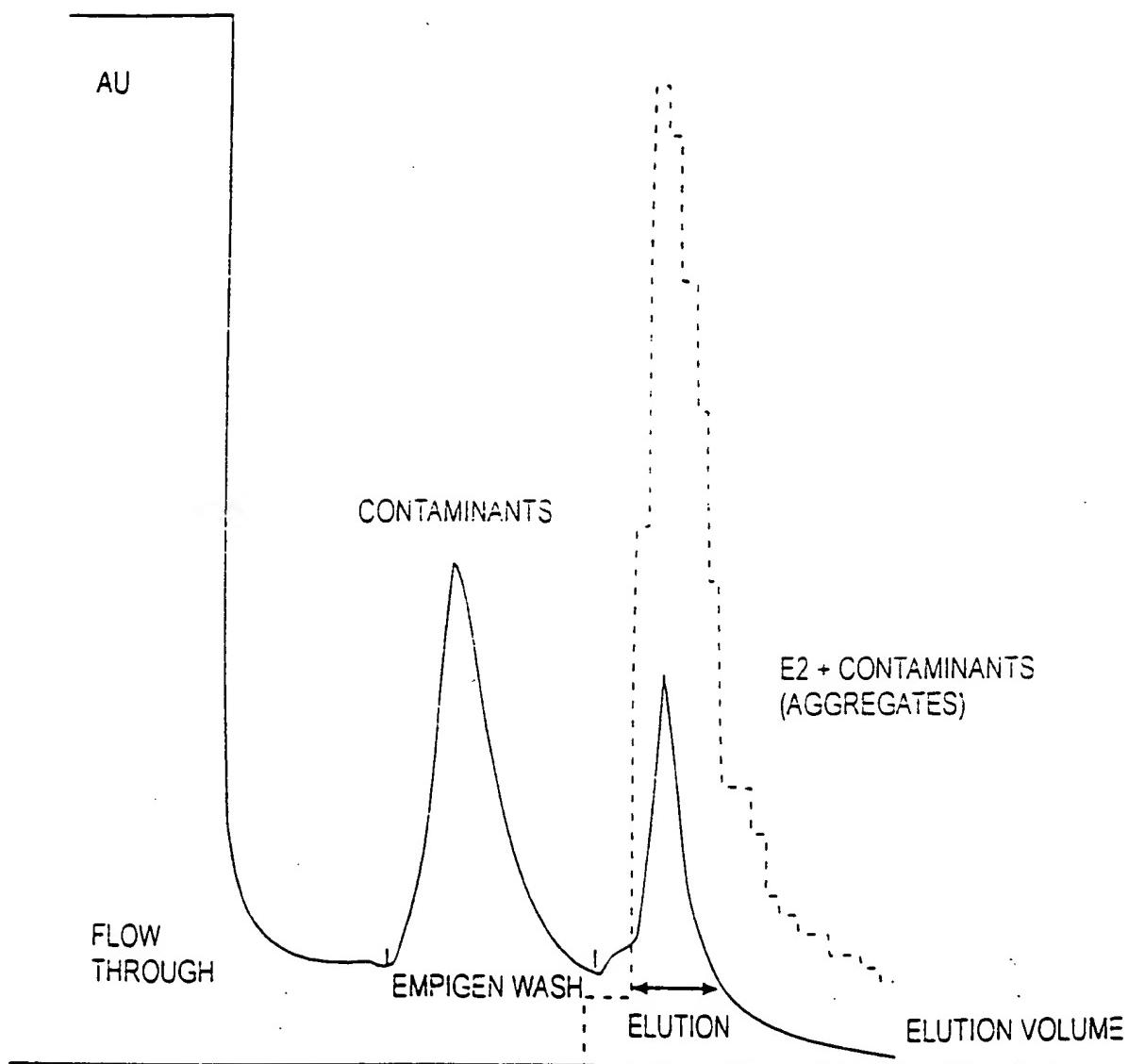
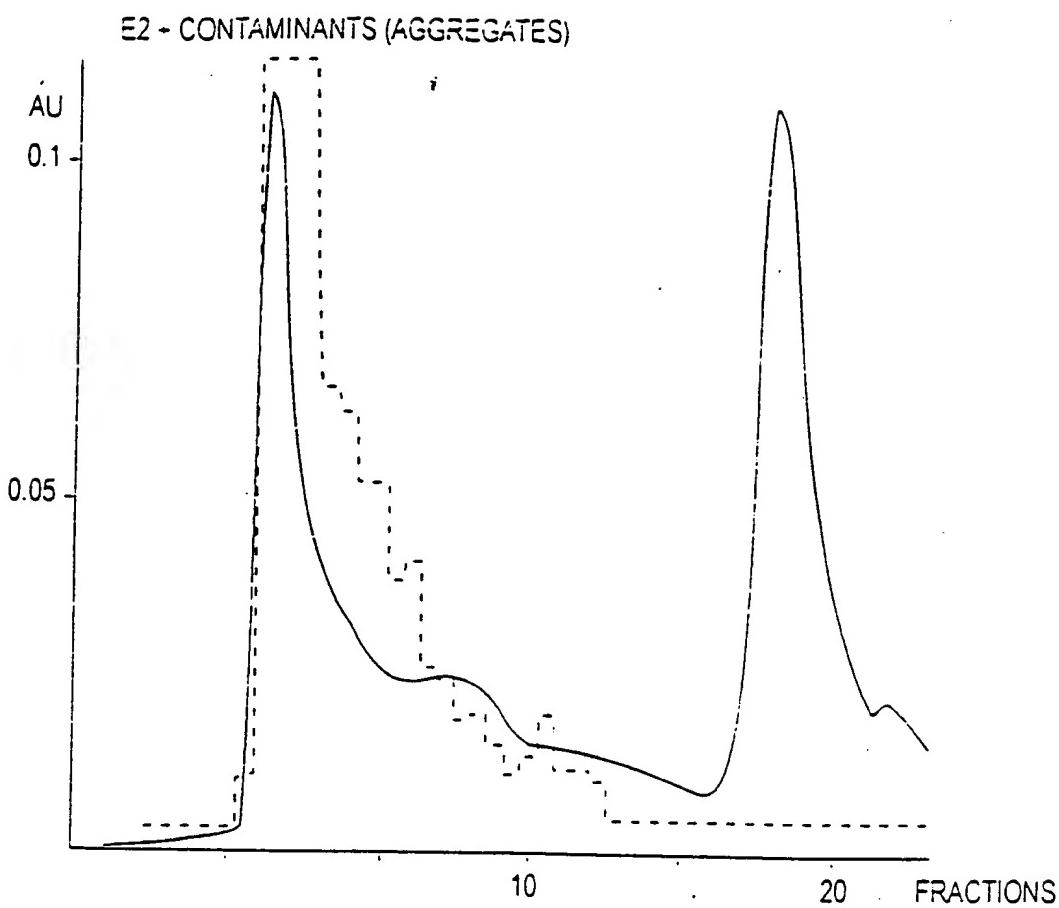


FIGURE 30

## A: NON - REDUCED



## B : REDUCED

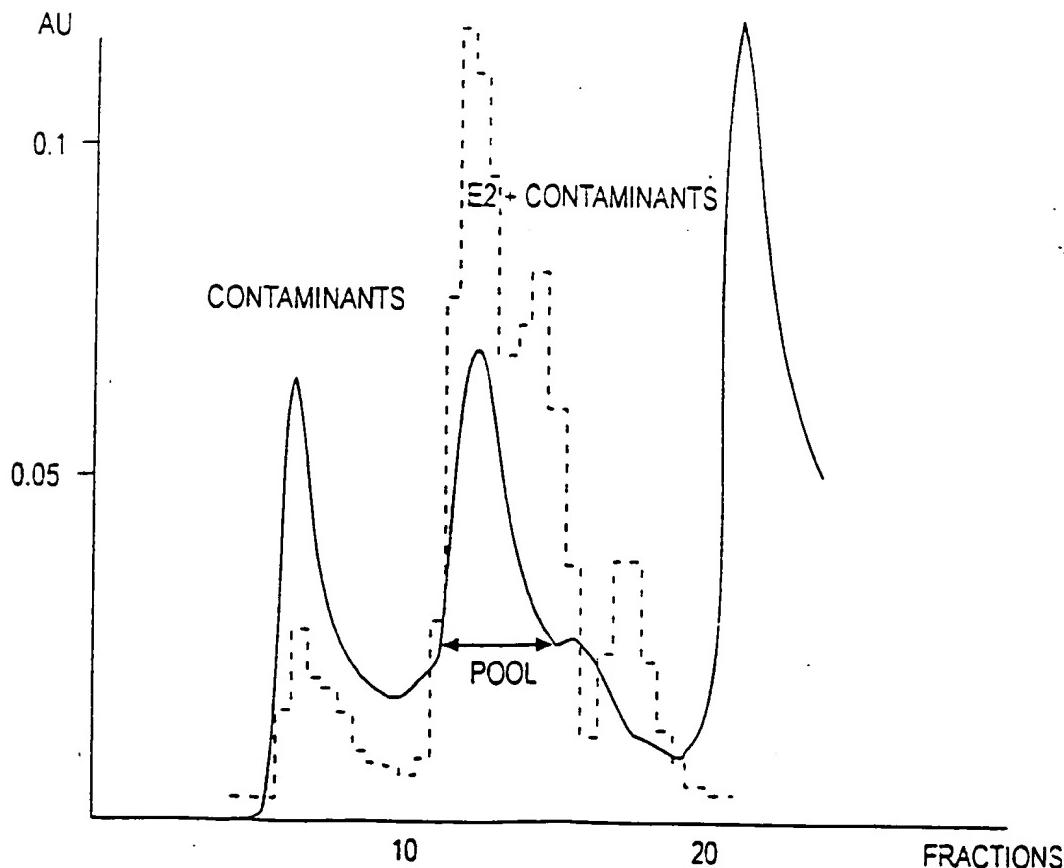


FIGURE 31

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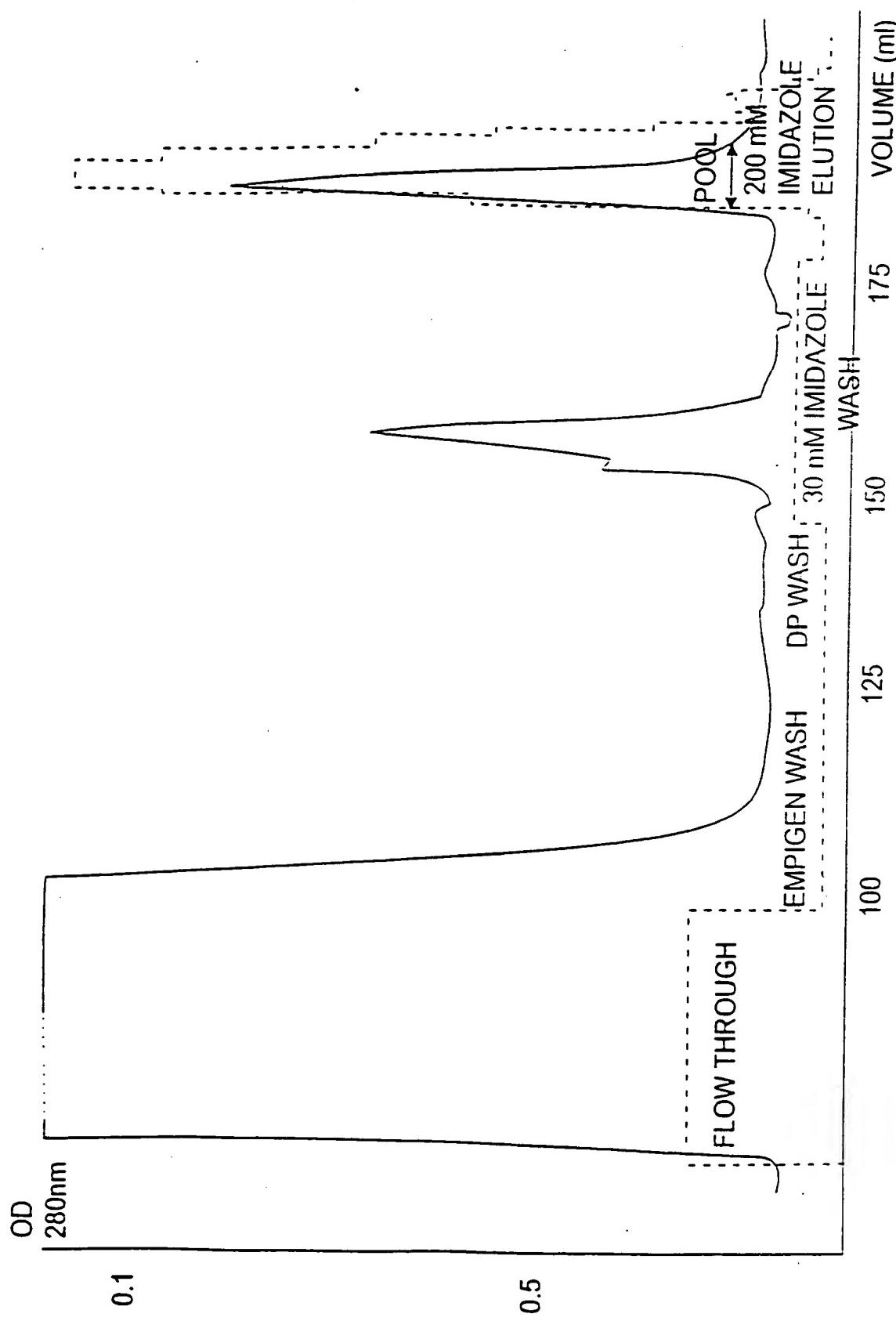
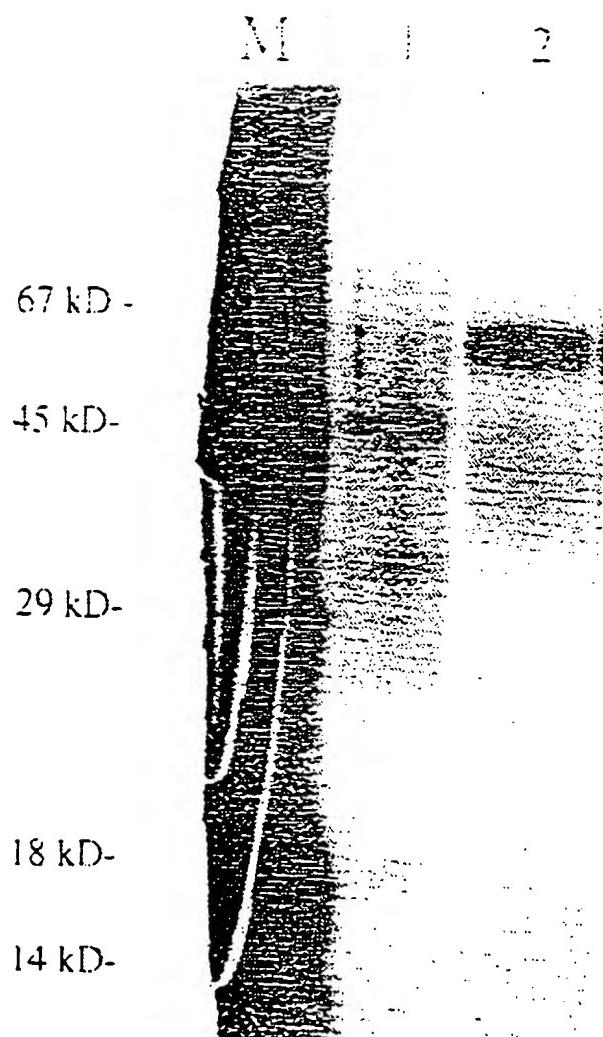


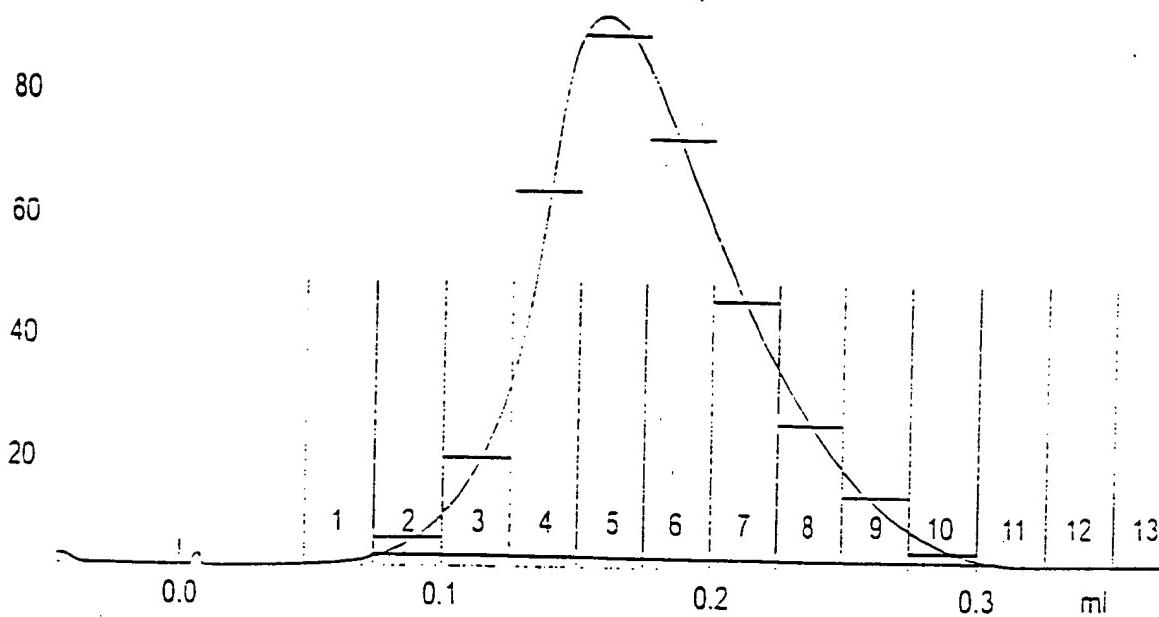
FIGURE 32

**FIGURE 33:**  
**SILVER STAIN OF PURIFIED E2**



1. 30 mM IMIDAZOLE WASH Ni-IMAC
2. 0.5  $\mu$ g E2

45 159 Figure 34



No.	Ret. (ml)	Peak start (ml)	Peak end (ml)	Dur (ml)	Area (ml <sup>2</sup> ·mAU)	Height (mAU)
1	-0.45	-0.46	-0.46	0.04	0.0976	4.579
2	1.55	0.75	3.26	2.51	796.4167	889.377
3	3.27	3.26	3.31	0.05	0.0067	0.224
4	3.33	3.32	3.33	0.02	0.0002	0.018

Total number of detected peaks = 4

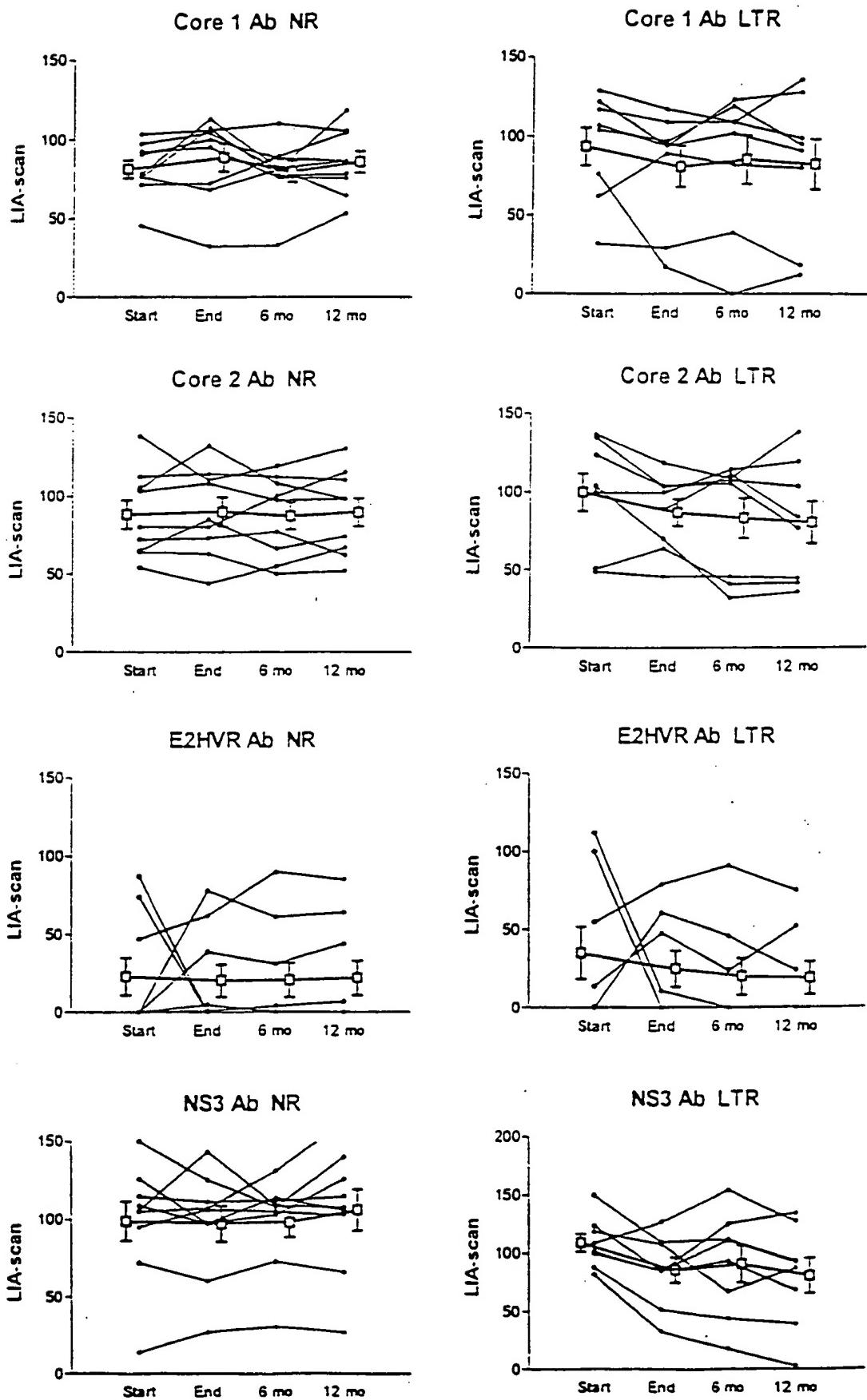
Total Area above baseline = 0.796522 ml<sup>2</sup>·AU

Total area in evaluated peaks = 0.796521 ml<sup>2</sup>·AU

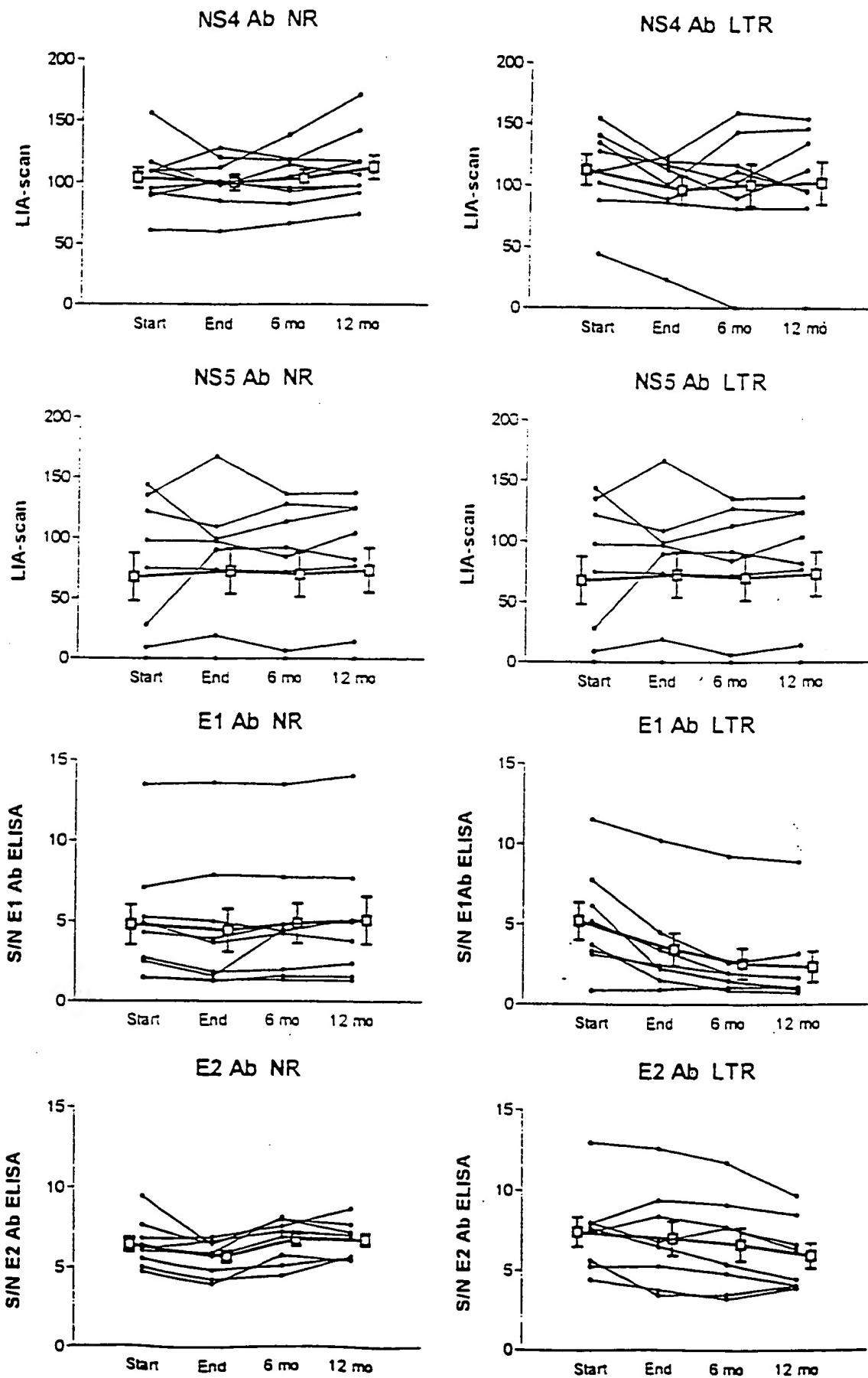
Ratio peak area / total area = 0.999999

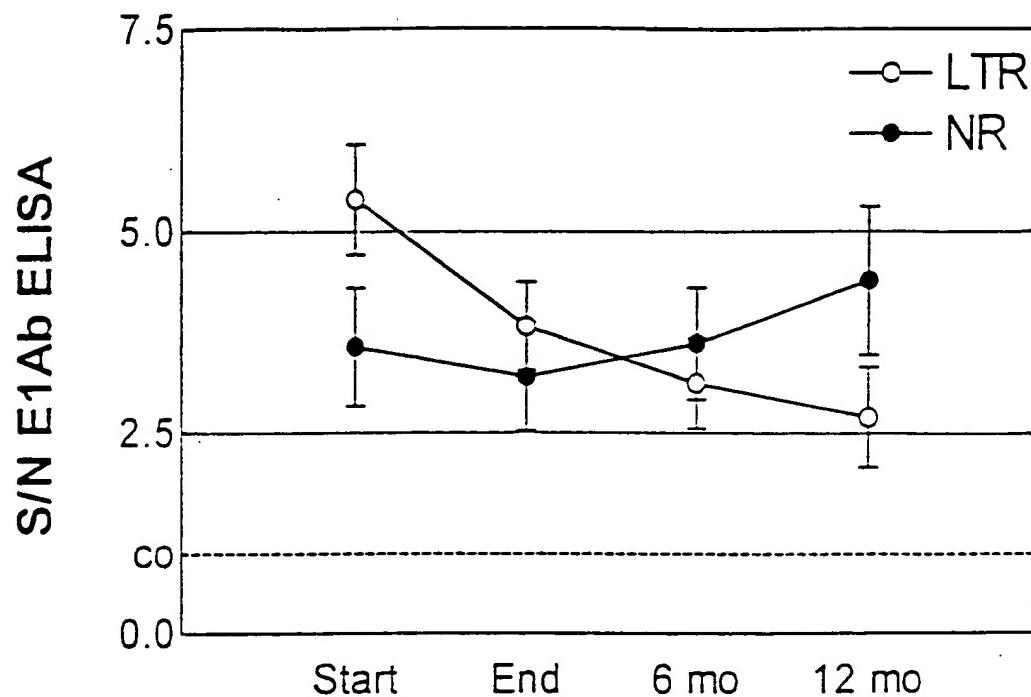
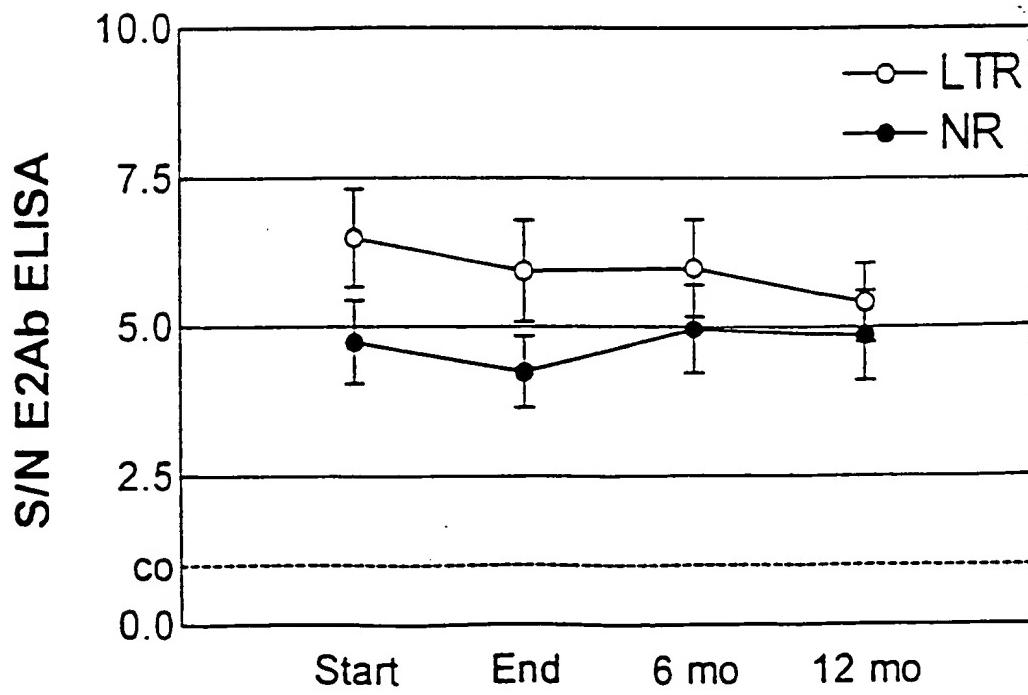
Total peak duration = 2.613583 ml

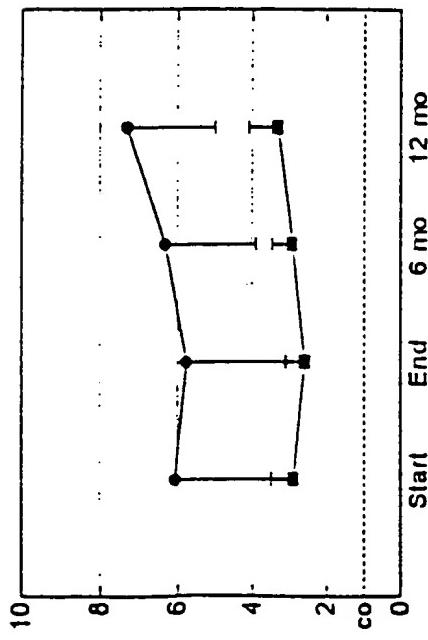
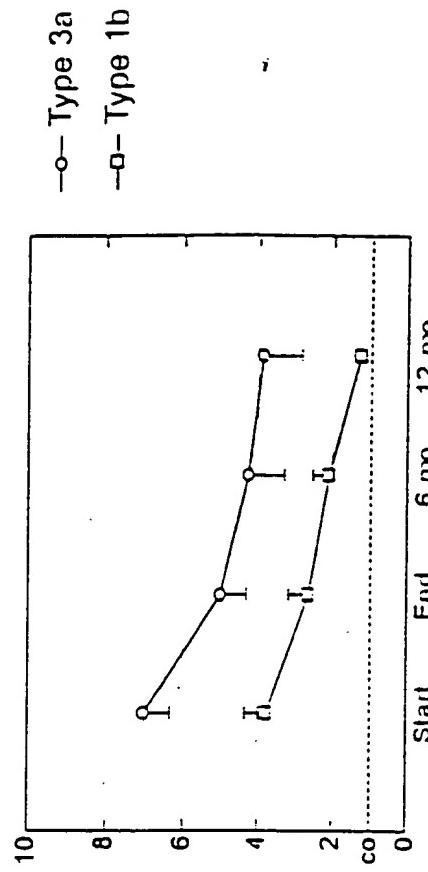
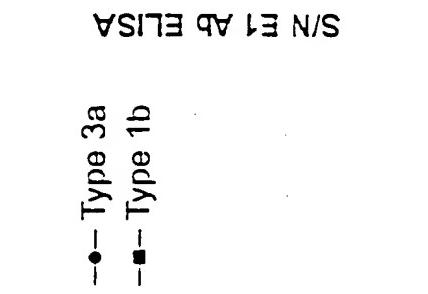
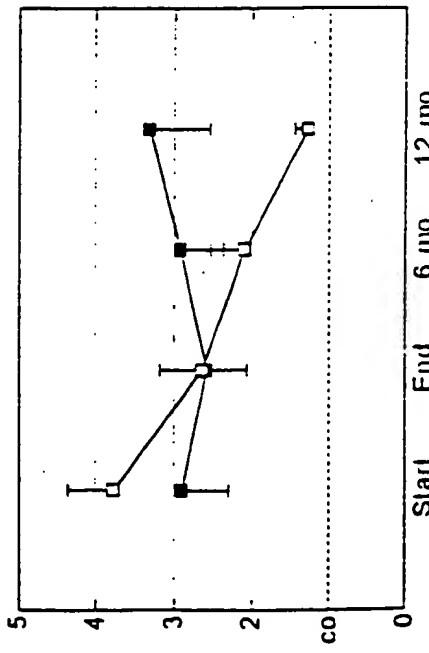
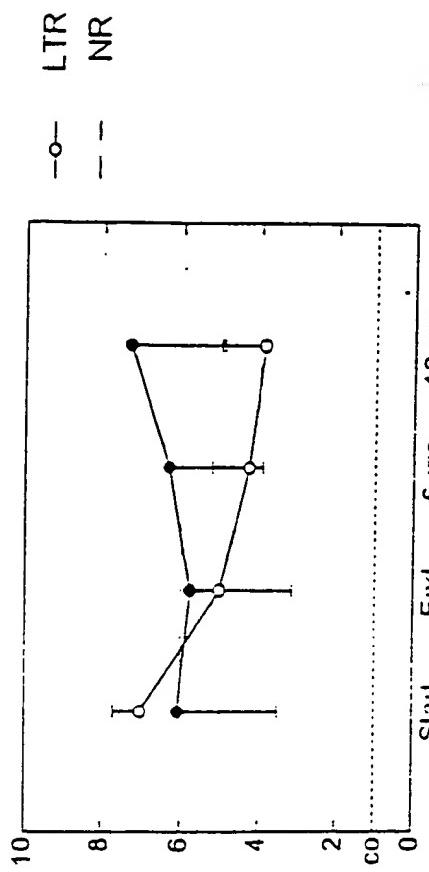
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**FIGURE 35A**



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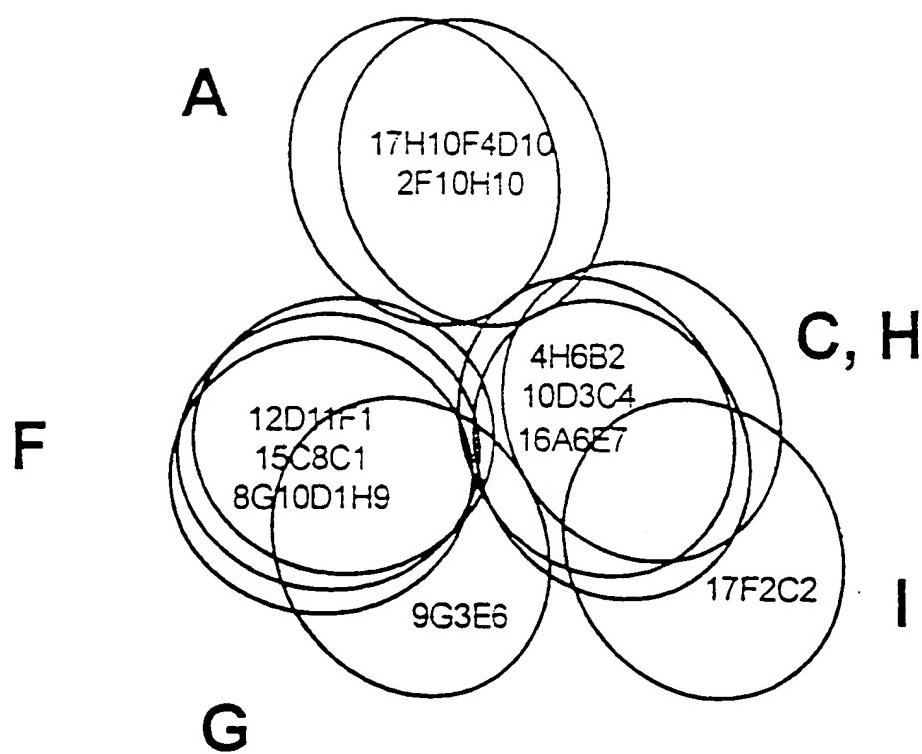
**FIGURE 35B**

<sup>48/59</sup>  
Figure 36**E1 Ab****E2 Ab**

**FIGURE 37****Non Responders****Long Term Responders****Type 1b****Type 3a**

# Figure 38

## Relative Map Positions of anti-E2 monoclonal antibodies



## PARTIAL DEGLYCOSYLATION OF HCV E1 ENVELOPE PROTEIN

## Endoglycosidase H (Endo H)

Lysopeptidase F  
(PNGase F)

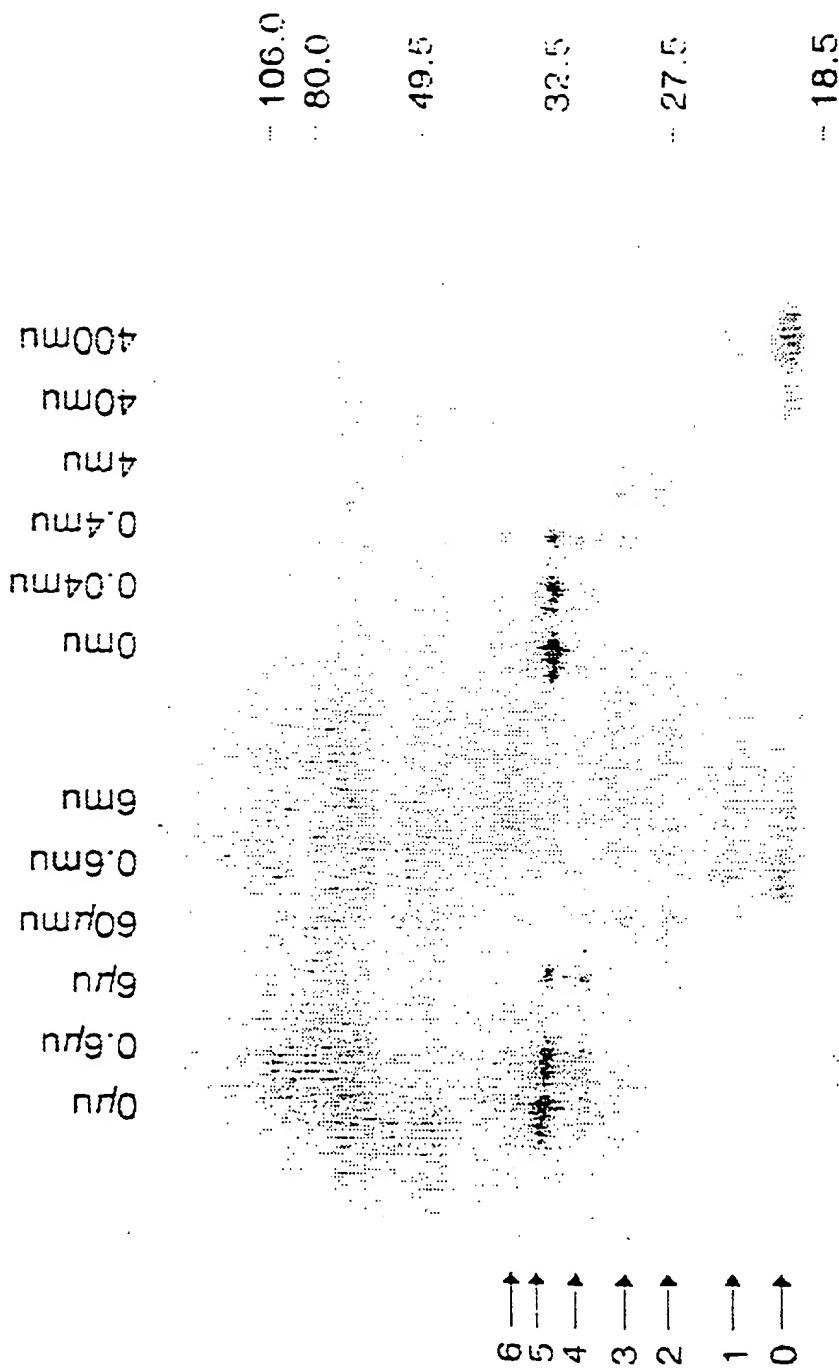
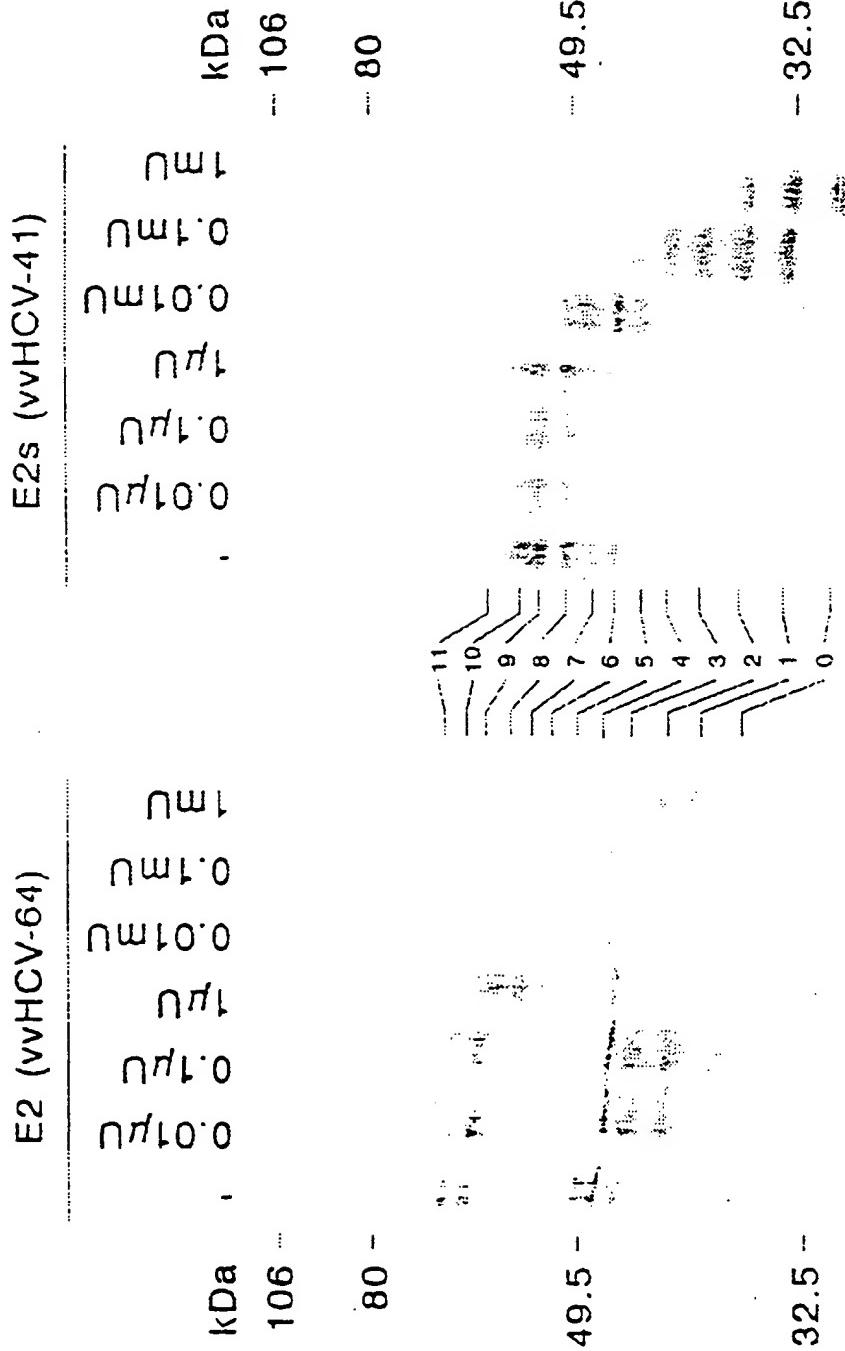


Figure 39

# PARTIAL TREATMENT OF HCV E2\E2s ENVELOPE PROTEINS BY PNGase F



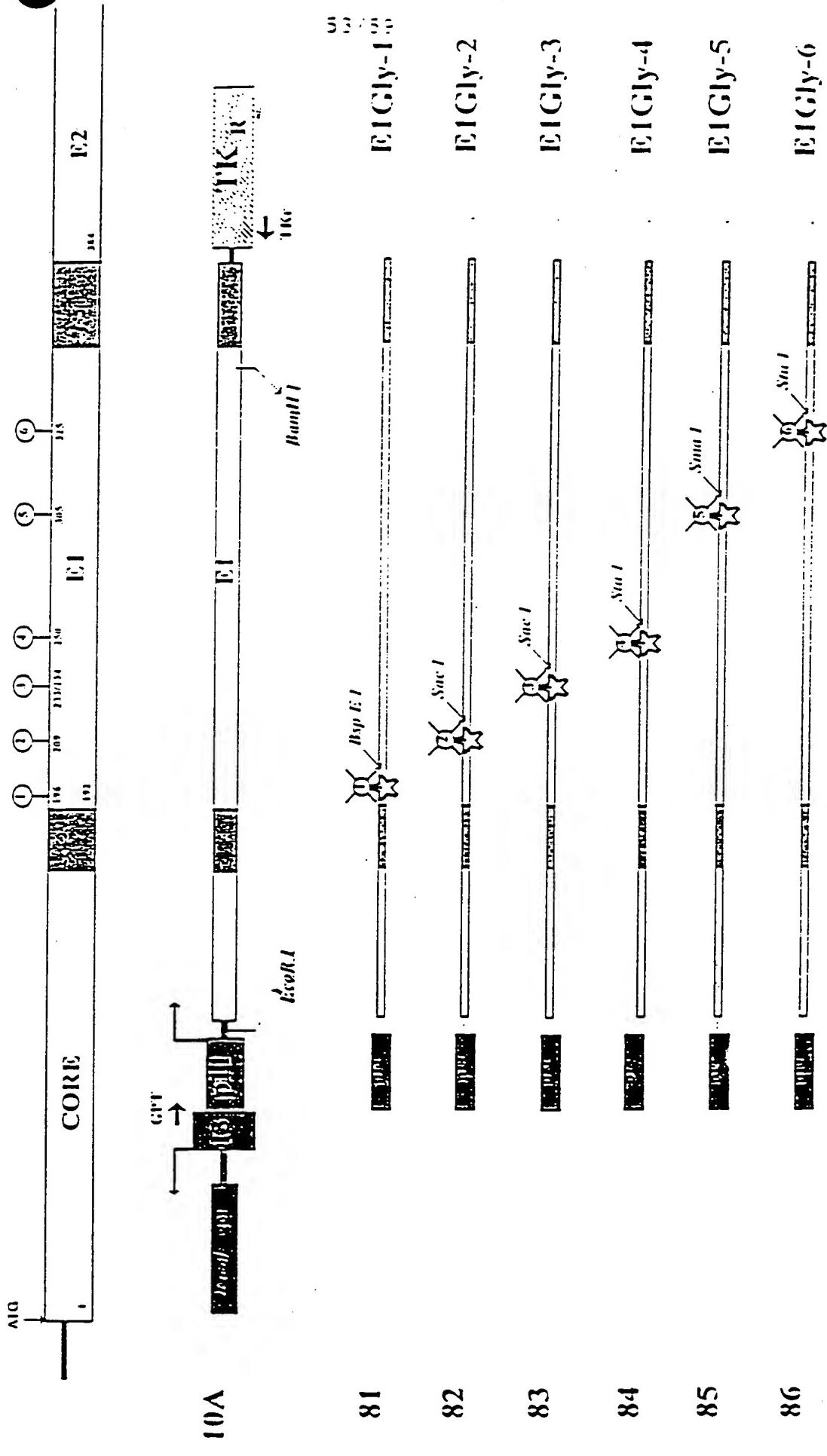
**Figure 40**

**Fig. 41**

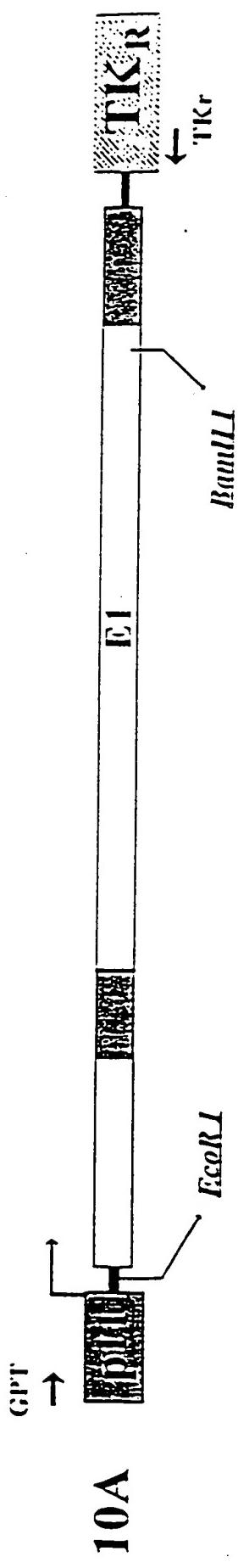
*In Vitro* Mutagenesis of IICV EI glycoprotein

WO 96/043

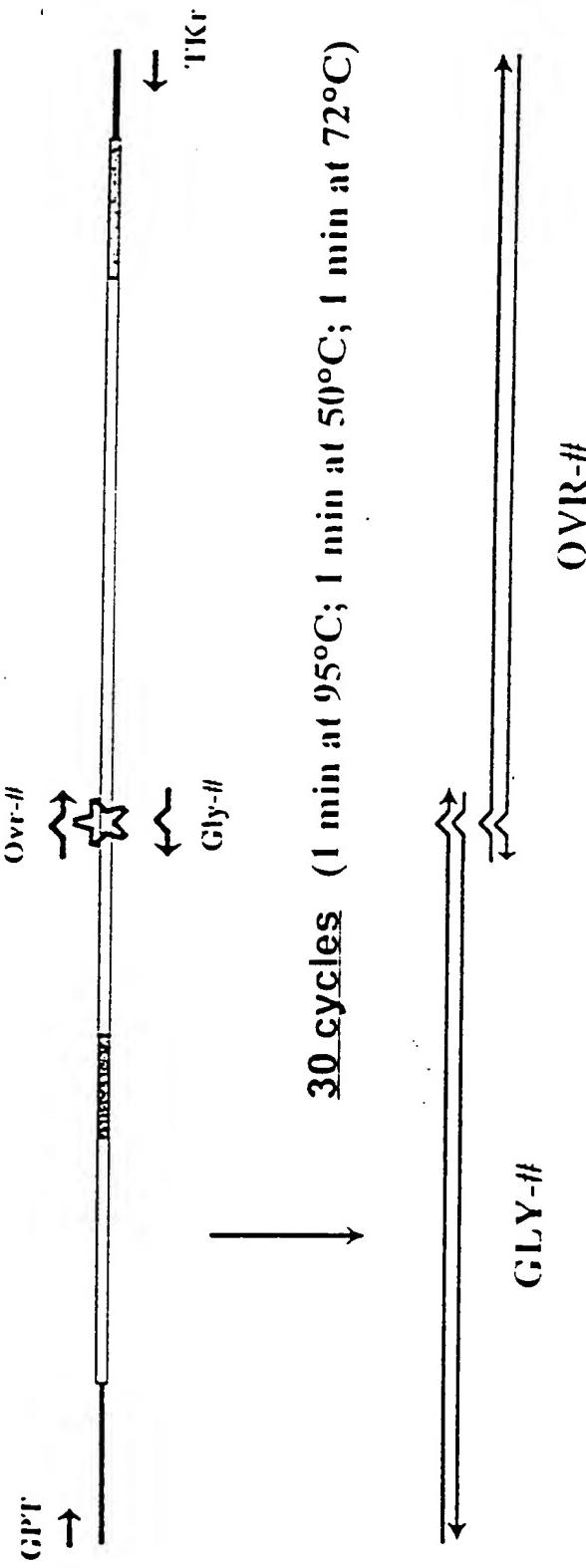
PCT/EP95/03031



**Fig. 42A      *In Vitro* Mutagenesis of HCV E1 glycoprotein**

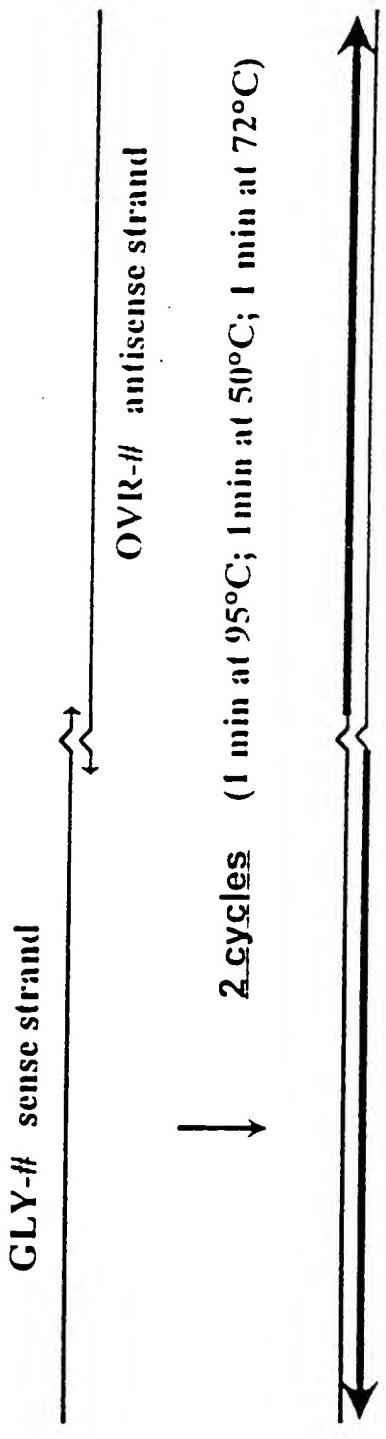


**1. First step of PCR amplification (Gly-#1 and Ovr-#1 primers)**



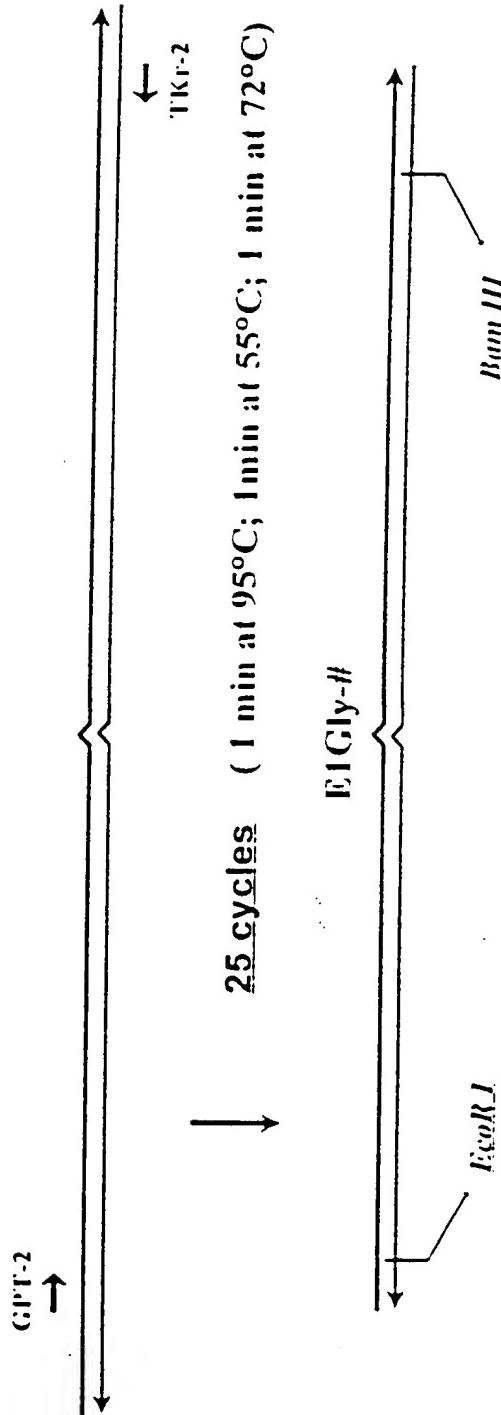
## 2. Overlap extension and nested PCR

### a. Overlap extension

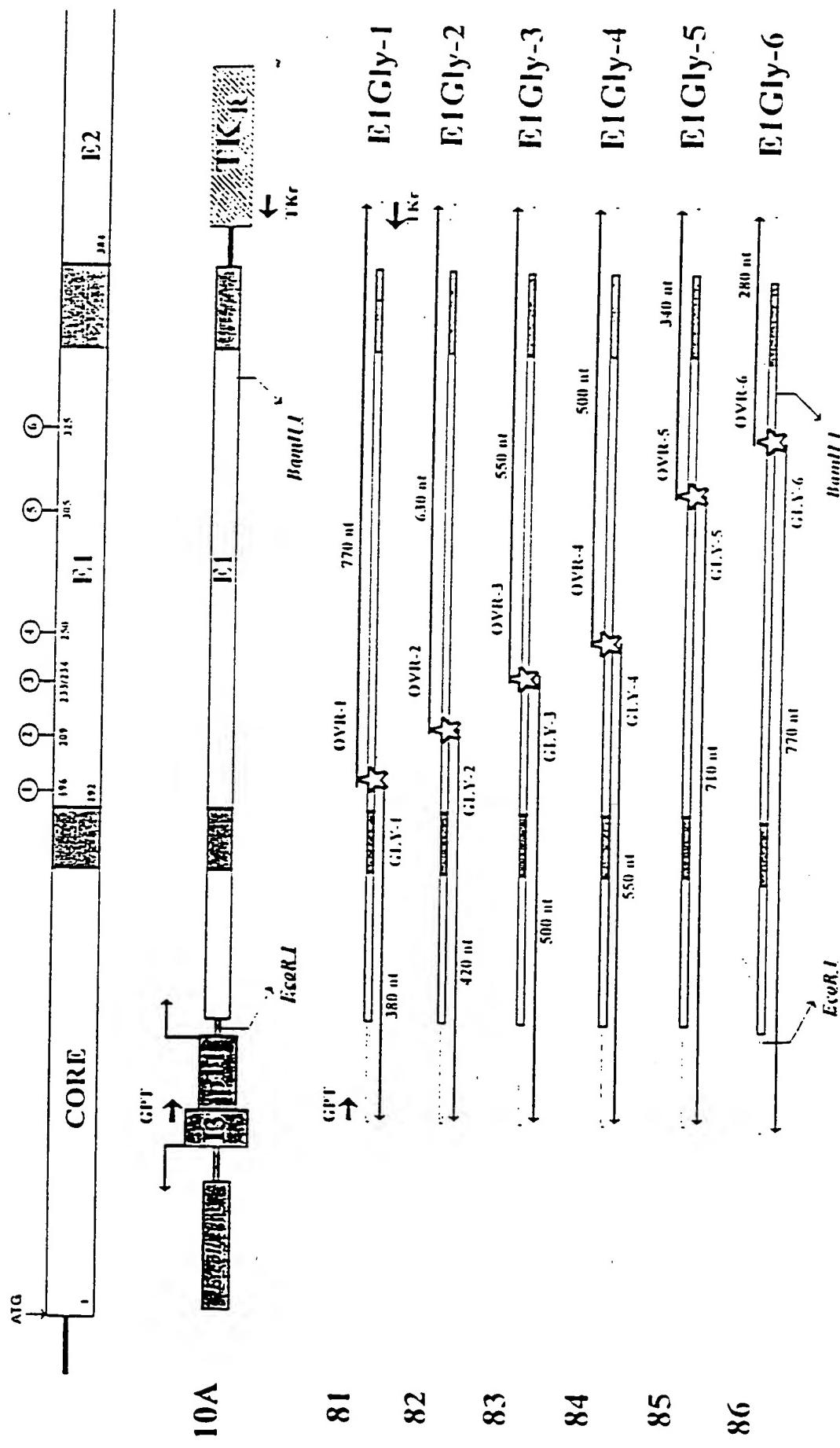


**Fig. 42B**

### b. Nested PCR amplification (GPT-2 and TKr-2 primers)



**Fig. 43 In Vitro Mutagenesis of HCV E1 glycoprotein**



		HeLa cells						RK 13 cells								
		1	2	3	4	5	6	7	2	1	3	4	5	6	7	
80.0	—								—	80.0					—	80.0
49.5	—								—	49.5					—	49.5
32.5	—								—	32.5					—	32.5
27.5	—								—	27.5					—	27.5
18.5	—								—	18.5					—	18.5

Figure 44A

00000000000000000000000000000000

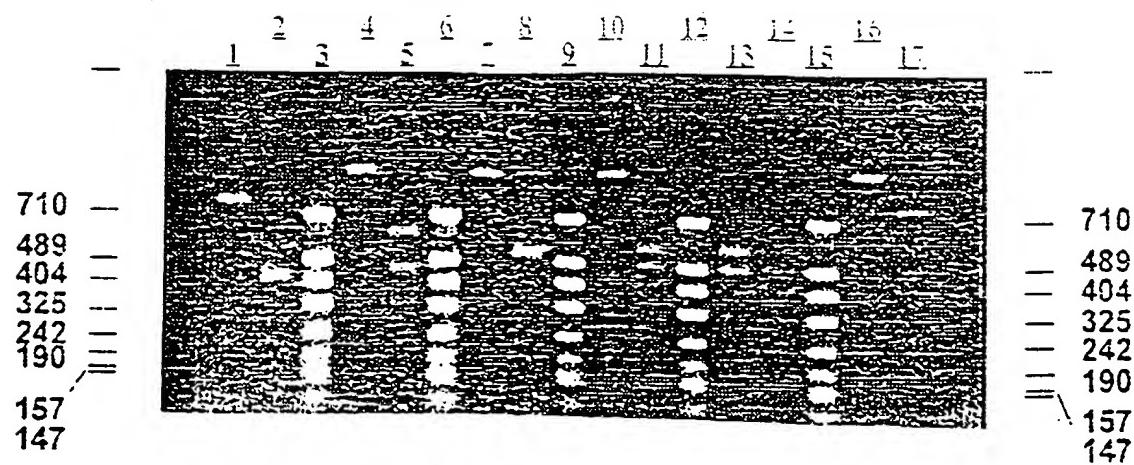


Figure 418



Figure 45

kDa

— 119

— 67

— 43

— 29

— 18



Figure 46